Risperidone (detailed)

Risperidone: Uses, Dosage, Side Effects

http://www.drugs.com/risperidone.html December 09, 2014

Risperidone is used to treat schizophrenia and symptoms of bipolar disorder. Learn about side effects, interactions and indications.

Risperidone is a antipsychotic medicine. It works by changing the effects of chemicals in the brain.

Risperidone is used to treat schizophrenia and symptoms of bipolar disorder (manic depression). It is also used in autistic children to treat symptoms of irritability.

Risperidone may also be used for purposes not listed in this medication guide.

Risperidone is not approved for use in psychotic conditions related to dementia. It may increase the risk of death in older adults with dementia-related conditions.

Do not give risperidone to a child without a doctor's advice.

While you are taking risperidone, you may be more sensitive to temperature extremes such as very hot or cold conditions. Avoid getting too cold, or becoming overheated or dehydrated. Drink plenty of fluids, especially in hot weather and during exercise. It is easier to become dangerously overheated and dehydrated while you are taking this medication.

Risperidone may impair your thinking or reactions. Be careful if you drive or do anything that requires you to be alert. Drinking alcohol can increase certain side effects of risperidone.

Stop using this medicine and call your doctor at once if you have fever, stiff muscles, confusion, sweating, fast or uneven heartbeats, restless muscle movements in your face or neck, tremor (uncontrolled shaking), trouble swallowing, feeling light-headed, or fainting.

You should not use risperidone if you are allergic to it.

Risperidone is not approved for use in psychotic conditions related to dementia. Risperidone may increase the risk of death in older adults with dementia-related conditions.

To make sure this medicine is safe for you, tell your doctor if you have:

Some people with mental illness have thoughts about suicide. Your doctor will need to check your progress at regular visits while you are using risperidone. Your family or other caregivers should also be alert to changes in your mood or symptoms.

The risperidone orally disintegrating tablet may contain phenylalanine. Talk to your doctor before using orally disintegrating tablets if you have phenylketonuria (PKU).

FDA pregnancy category C. It is not known whether risperidone will harm an unborn baby. Tell your doctor if you are pregnant or plan to become pregnant while taking risperidone or within 12 weeks after you stop taking this medicine.

See also: Pregnancy and breastfeeding warnings (in more detail)

Taking antipsychotic medication during the last 3 months of pregnancy may cause problems in the newborn, such as withdrawal symptoms, breathing problems, feeding problems, fussiness, tremors, and limp or stiff muscles. However, you may have withdrawal symptoms or other problems if you stop taking your medicine during pregnancy. If you become pregnant while taking this medicine, do not stop taking it without your doctor's advice.

Risperidone can pass into breast milk and may harm a nursing baby. Do not breast-feed while taking this medicine and for at least 12 weeks after your treatment ends.

Do not give this medicine to a child without a doctor's advice.

Take risperidone exactly as prescribed by your doctor. Follow all directions on your prescription label. Do not take this medicine in larger or smaller amounts or for longer than recommended.

Risperidone can be taken with or without food.

To take the orally disintegrating tablet (Risperdal M-Tabs):

Measure liquid medicine with the dosing syringe provided, or with a special dose-measuring spoon or medicine cup. If you do not have a dose-measuring device, ask your pharmacist for one.

Use risperidone regularly to get the most benefit. Get your prescription refilled before you run out of medicine completely.

Do not mix the liquid medicine with cola or tea.

It may take up to several weeks before your symptoms improve. Keep using the medication as directed and tell your doctor if your symptoms do not improve.

Store at room temperature away from moisture, heat, and light. Do not liquid medicine to freeze.

Take the missed dose as soon as you remember. Skip the missed dose if it is almost time for your next scheduled dose. Do not take extra medicine to make up the missed dose.

Seek emergency medical attention or call the Poison Help line at 1-800-222-1222.

Overdose symptoms may include severe drowsiness, fast heart rate, feeling light-headed, fainting, and restless muscle movements in your eyes, tongue, jaw, or neck.

Risperidone may impair your thinking or reactions. Be careful if you drive or do anything that requires you to be alert.

Avoid getting up too fast from a sitting or lying position, or you may feel dizzy. Get up slowly and steady yourself to prevent a fall.

Drinking alcohol can increase certain side effects of risperidone.

While you are taking this medicine, you may be more sensitive to temperature extremes such as very hot or cold conditions. Avoid getting too cold, or becoming overheated or dehydrated. Drink plenty of fluids, especially in hot weather and during exercise.

Get emergency medical help if you have any of these signs of an allergic reaction to risperidone: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

Call your doctor at once if you have:

This is not a complete list of side effects and others may occur. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

See also: Side effects (in more detail)

Taking this medicine with other drugs that make you sleepy can worsen this effect. Ask your doctor before taking risperidone with a sleeping pill, narcotic pain medicine, muscle relaxer, or medicine for anxiety, depression, or seizures.

Other drugs may interact with risperidone, including prescription and over-the-counter medicines, vitamins, and herbal products. Tell each of your health care providers about all medicines you use now and any medicine you start or stop using.

Wikipedia, the free encyclopedia

http://en.wikipedia.org/wiki/Risperidone December 09, 2014

Risperidone (trade name Risperdal, and generics) is an antipsychotic drug mainly used to treat schizophrenia (including adolescent schizophrenia), schizoaffective ...

Risperidone (// ri-SPAIR-i-dohn) (trade name Risperdal, and generics) is an antipsychotic drug mainly used to treat schizophrenia (including adolescent schizophrenia), schizoaffective disorder, the mixed and manic states of bipolar disorder, and irritability in people with autism.

Risperidone is a second-generation atypical antipsychotic.[2] It is a dopamine antagonist possessing anti-serotonergic, anti-adrenergic and anti-histaminergic properties.

Adverse effects of risperidone include significant weight gain and metabolic problems such as diabetes mellitus type 2,[3] as well as tardive dyskinesia and neuroleptic malignant syndrome. Risperidone and other antipsychotics also increase the risk of death in people with dementia.[4]

The drug was developed by Janssen-Cilag, subsidiary of Johnson & Johnson, from 1988 to 1992 as an improvement from the typical antipsychotic and first approved by the FDA in 1994.[5] Today many generic versions are available. It is on the World Health Organization's List of Essential Medicines, a list of the most important medication needed in a basic health system.[6]

Risperidone is used for the treatment of schizophrenia, bipolar disorder also including behavior problems in autistic people.[7]

Risperidone is effective in treating the acute exacerbations of schizophrenia.[8][9]

Studies evaluating the utility of the oral form of risperidone for maintenance therapy have reached varying conclusions. A 2012 systematic review concluded that there is strong evidence that risperidone is more effective than all first generation antipsychotics other than haloperidol, but that evidence directly supporting its superiority to placebo is equivocal.[10] A 2011 review concluded that risperidone is more effective in relapse prevention than other first and second generation antipsychotics with the exception of olanzapine and clozapine.[11] A 2010 Cochrane review found a slight benefit during the first few weeks of treatment of schizophrenia but the article raised concerns regarding bias favoring risperidone.[12]

Long-acting injectable formulations of antipsychotic drugs provide improved compliance with therapy and reduce relapse rates relative to oral formulations.[13][14] The efficacy of risperidone long acting injection appears to be similar to that of long acting injectable forms of first generation antipsychotics.[15]

Second generation antipsychotics, including risperidone, are effective in the treatment of manic symptoms in acute manic or mixed exacerbations of bipolar disorder.[16][17][18] In children and adolescents, risperidone may be more effective than lithium or divalproex, but has more metabolic side effects.[19] As maintenance therapy, aripiprazole is effective for the prevention of manic episodes but not depression.[20] The long-acting injectable form of risperidone may be advantageous over long acting first generation antipsychotics, as it is better tolerated (fewer extrapyramidal effects) and because long acting injectable formulations of first generation antipsychotics may increase the risk of depression.[21]

Compared to placebo, risperidone treatment reduces certain problematic behaviors in autistic children, including aggression toward others, self-injury, temper tantrums, and rapid mood changes. The evidence for its efficacy appears to be greater than that for alternative pharmacological treatments.[22]Weight gain is an important adverse effect.[23][24] Some authors recommend limiting the use of aripiprazole to those with the most challenging behavioral disturbances in order to minimize the risk of drug-induced adverse effects.[25] Evidence for the efficacy of risperidone in autistic adolescents and young adults is less persuasive.[26]

Risperidone provides no benefit in the treatment of eating disorders or personality disorders.[27]

While antipsychotic medications such as risperidone have a slight benefit in people with dementia, they have been linked to higher incidences of death and stroke.[27] Because of this increased risk of death, treatment of dementia-related psychosis with risperidone is not FDA approved.[28]

The British National Formulary recommends a gradual withdrawal when discontinuing antipsychotic treatment to avoid acute withdrawal syndrome or rapid relapse.[31] Some have argued the additional somatic and psychiatric symptoms associated with dopaminergic super-sensitivity, including dyskinesia and acute psychosis, are common features of withdrawal in individuals treated with neuroleptics.[32][33][34][35] This has led some to suggest the withdrawal process might itself be schizomimetic, producing schizophrenia-like symptoms even in previously healthy patients, indicating a possible pharmacological

origin of mental illness in a yet unknown percentage of patients currently and previously treated with antipsychotics. This question is unresolved, and remains a highly controversial issue among professionals in the medical and mental health communities, as well the public.[36]

Older people with dementia-related psychosis are at a higher risk of death if they take risperidone compared to those who do not. Most deaths are related to heart problems or infections.[30]

Risperidone is available as an oral tablet, oral dissolving tablet, or intramuscular injection.[7] The intramuscular preparation, marketed as Risperdal Consta, can be given once every two weeks. It is slowly released from the injection site. This method of administration may be used on sanctioned patients (detained), who are refusing, or consenting patients who may have disorganized thinking and cannot remember to take their daily doses.[37]

Risperidone undergoes hepatic metabolism and renal excretion. Lower doses are recommended for patients with severe liver and kidney disease.[28]

Risperidone belongs as a chemical structure to a new antipsychotic medication chemical group called "benzioxazoles".

Risperidone has been classified as a "qualitatively atypical" antipsychotic agent with a relatively low incidence of extrapyramidal side effects (when given at low doses) that has more pronounced serotonin antagonism than dopamine antagonism. It has actions at several 5-HT (serotonin) receptor subtypes. These are 5-HT , linked to weight gain, 5-HT , linked to its antipsychotic action and relief of some of the extrapyramidal side effects experienced with the typical neuroleptics.[38]

It was recently found that D-amino acid oxidase, the enzyme that catalyses the breakdown of D-amino acids (e.g. D-alanine and D-serine — the neurotransmitters) is inhibited by risperidone.[39]

Risperidone acts on the following receptors:

Dopamine receptors: This drug is an antagonist of the D1 (D1, and D5) as well as the D2 family (D2, D3 and D4) receptors. This drug has "tight binding" properties, which means it has a long half-life and like other antipsychotics, risperidone blocks the mesolimbic pathway, the prefrontal cortex limbic pathway, and the tuberoinfundibular pathway in the central nervous system. Risperidone may induce extrapyramidal side effects, akathisia and tremors, associated with diminished dopaminergic activity in the striatum. It can also cause sexual side effects, galactorrhoea, infertility, gynecomastia and, with chronic use reduced bone mineral density leading to breaks all of which are associated with increased prolactin secretion.[38]

Serotonin receptors: Its action at these receptors may be responsible for its lower extrapyramidal side effect liability (via the 5-HT receptors) and improved negative symptom control compared to typical antipsychotics such as haloperidol for instance. Its antagonistic actions at the 5-HT receptor may account, in part, for its weight gain liability.

Alpha α1 adrenergic receptors: This action accounts for its orthostatic hypotensive effects and perhaps some of the sedating effects of risperidone.[38]

Histamine H1 receptors: effects on these receptors account for its sedation and reduction in vigilance. This may also lead to drowsiness and weight gain.[38]

Though this medication possesses similar effects to other typical and atypical antipsychotics, it does not possess an affinity for the muscarinic acetylcholine receptors. In many respects, this medication can be useful as an "acetylcholine release-promoter" similar to gastrointestinal drugs such as metoclopramide and cisapride.

Risperidone was approved by the United States Food and Drug Administration (FDA) in 1994 for the treatment of schizophrenia.[42] On August 22, 2007, risperidone was approved as the only drug agent available for treatment of schizophrenia in youths, ages 13–17; it was also approved that same day for treatment of bipolar disorder in youths and children, ages 10–17, joining lithium. Risperidone contains the functional groups of benzisoxazole and piperidine as part of its molecular structure. Although not a butyrophenone, it was developed with the structures of benperidol and ketanserin as a basis. In 2003, the FDA approved risperidone for the short-term treatment of the mixed and manic states associated with bipolar disorder. In 2006, the FDA approved risperidone for the treatment of irritability in autistic

children and adolescents.[43] The FDA's decision was based in part on a study of autistic people with severe and enduring problems of violent meltdowns, aggression, and self-injury; risperidone is not recommended for autistic people with mild aggression and explosive behavior without an enduring pattern.[44]

Janssen's patent on risperidone expired on December 29, 2003, opening the market for cheaper generic versions from other companies, and Janssen's exclusive marketing rights expired on June 29, 2004 (the result of a pediatric extension).

Risperidone is available as a tablet, an oral solution, and an ampule, Risperdal Consta, which is a depot injection administered once every two weeks. It is also available as a wafer known in the United States and Canada as Risperdal M-Tabs and elsewhere as Risperdal Quicklets. Risperidone is also available as paliperidone IM injections (a risperidone derivative). This injection is given 12 times a year on the same day each month.

Risperidone became available as a generic drug in October 2008 from Teva Pharmaceuticals, Dr. Reddy's Laboratories, Inc. and Patriot Pharmaceutics. The Patriot generic is an authorized generic pharmaceutical. The drug is currently marketed in India under several brand names including Risperdal, Risdon and Sizodon.

On 11 April 2012, Johnson & Johnson and its subsidiary Janssen Pharmaceuticals Inc. were fined $1.2 billion by Judge Timothy Davis Fox of the Sixth Division of the Sixth Judicial Circuit of the U.S. state of Arkansas.[45] The jury found the companies had downplayed multiple risks associated with risperidone (Risperdal). The verdict was later reversed by the Arkansas State Supreme court.[46]

According to the Wall Street Journal on June 20, 2012, "Johnson & Johnson and the U.S. Justice Department [we]re close to settling a protracted investigation into the company’s promotion of the antipsychotic Risperdal, for what would be one of the highest sums to date in a drug-marketing case. The sides are trying to wrap together a number of lawsuits, state investigations and other probes of alleged illegal marketing, and are discussing a payment of $1.5 billion or higher." The fine ultimately imposed totaled $2.2 billion.[47]

In August 2012, Johnson & Johnson agreed to pay $181 million to 36 U.S. states in order to settle claims that it had promoted risperidone for off-label uses including for dementia, anger management, and anxiety.[48]

MedlinePlus Drug Information

http://www.nlm.nih.gov/medlineplus/druginfo/meds/a694015.html December 09, 2014

Risperidone comes as a tablet, a solution (liquid), and an orally disintegrating tablet (tablet that dissolves quickly in the mouth) to take by mouth.

Studies have shown that older adults with dementia (a brain disorder that affects the ability to remember, think clearly, communicate, and perform daily activities and that may cause changes in mood and personality) who take antipsychotics (medications for mental illness) such as risperidone have an increased risk of death during treatment. Older adults with dementia may also have a greater chance of having a stroke or mini-stroke during treatment. Tell your doctor and pharmacist if you are taking furosemide (Lasix). Risperidone is not approved by the Food and Drug Administration (FDA) for the treatment of behavior problems in older adults with dementia. Talk to the doctor who prescribed this medication if you, a family member, or someone you care for has dementia and is taking risperidone. For more information visit the FDA website: http://www.fda.gov/Drugs

Why is this medication prescribed?

Risperidone is used to treat the symptoms of schizophrenia (a mental illness that causes disturbed or unusual thinking, loss of interest in life, and strong or inappropriate emotions) in adults and teenagers 13 years of age and older. It is also used to treat episodes of mania (frenzied, abnormally excited, or irritated mood) or mixed episodes (symptoms of mania and depression that happen together) in adults and in teenagers and children 10 years of age and older with bipolar disorder (manic depressive disorder; a disease that causes episodes of depression, episodes of mania, and other abnormal moods). Risperidone is also used to treat behavior problems such as aggression, self-injury, and sudden mood changes in teenagers and children 5 to 16 years of age who have autism (a condition that causes

repetitive behavior, difficulty interacting with others, and problems with communication). Risperidone is in a class of medications called atypical antipsychotics. It works by changing the activity of certain natural substances in the brain.

How should this medicine be used?

Risperidone comes as a tablet, a solution (liquid), and an orally disintegrating tablet (tablet that dissolves quickly in the mouth) to take by mouth. It is usually taken once or twice a day with or without food. Take risperidone at around the same time(s) every day. Follow the directions on your prescription label carefully, and ask your doctor or pharmacist to explain any part you do not understand. Take risperidone exactly as directed. Do not take more or less of it or take it more often than prescribed by your doctor.

Use the dropper provided to measure your dose of risperidone oral solution. You can take the oral solution with water, orange juice, coffee, or low-fat milk. Do not take the solution with tea or cola.

Do not try to push the orally disintegrating tablet through the foil. Instead, use dry hands to peel back the foil packaging. Immediately take out the tablet and place it on your tongue. The tablet will quickly dissolve and can be swallowed with or without liquid. Do not chew or crush the tablet.

Your doctor will probably start you on a low dose of risperidone and gradually increase your dose to allow your body to adjust to the medication.

Risperidone may help control your symptoms but will not cure your condition. It may take several weeks or longer before you feel the full benefit of risperidone. Continue to take risperidone even if you feel well. Do not stop taking risperidone without talking to your doctor. If you suddenly stop taking risperidone, your symptoms may return and your illness may become harder to treat.

This medication may be prescribed for other uses; ask your doctor or pharmacist for more information.

Unless your doctor tells you otherwise, continue your normal diet.

Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

Risperidone may cause children to gain more weight than expected and for boys and male teenagers to have an increase in the size of their breasts. Talk to your doctor about the risks of giving this medication to your child.

Risperidone may cause other side effects. Call your doctor if you have any unusual problems while taking this medication.

If you experience a serious side effect, you or your doctor may send a report to the Food and Drug Administration's (FDA) MedWatch Adverse Event Reporting program online [at http://www.fda.gov/Safety/MedWatch] or by phone [1-800-332-1088].

Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom). Always store the orally disintegrating tablets in their sealed package, and use them immediately after opening the package. Throw away any medication that is outdated or no longer needed. Talk to your pharmacist about the proper disposal of your medication.

In case of overdose, call your local poison control center at 1-800-222-1222. If the victim has collapsed or is not breathing, call local emergency services at 911.

Keep all appointments with your doctor and the laboratory. Your doctor may order certain lab tests to check your body's response to risperidone.

Do not let anyone else take your medication. Ask your pharmacist any questions you have about refilling your prescription.

It is important for you to keep a written list of all of the prescription and nonprescription (over-the-counter) medicines you are taking, as well as any products such as vitamins, minerals, or other dietary

supplements. You should bring this list with you each time you visit a doctor or if you are admitted to a hospital. It is also important information to carry with you in case of emergencies.

FDA prescribing information, side effects and uses

http://www.drugs.com/pro/risperidone.html December 09, 2014

Risperidone official prescribing information for healthcare professionals. Includes: indications, dosage, adverse reactions, pharmacology and more.

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Risperidone is not approved for the treatment of patients with dementia-related psychosis. [See Warnings and Precautions (5.1)]

Risperidone tablets USP are indicated for the treatment of irritability associated with autistic disorder, including symptoms of aggression towards others, deliberate self-injuriousness, temper tantrums, and quickly changing moods. Efficacy was established in 3 short-term trials in children and adolescents (ages 5 to 17 years) [see Clinical Studies (14.4)].

Risperidone tablets USP adjunctive therapy with lithium or valproate is indicated for the treatment of acute manic or mixed episodes associated with Bipolar I Disorder. Efficacy was established in one short-term trial in adults [see Clinical Studies (14.3)].

Risperidone tablets USP are indicated for the treatment of acute manic or mixed episodes associated with Bipolar I Disorder. Efficacy was established in 2 short-term trials in adults and one short-term trial in children and adolescents (ages 10 to 17 years) [see Clinical Studies (14.2)].

Risperidone tablets USP are indicated for the treatment of schizophrenia. Efficacy was established in 4 short-term trials in adults, 2 short-term trials in adolescents (ages 13 to 17 years), and one long-term maintenance trial in adults [see Clinical Studies (14.1)].

When fluoxetine or paroxetine is coadministered with Risperidone tablets, the dose of Risperidone tablets should be reduced. The Risperidone tablet dose should not exceed 8 mg per day in adults when coadministered with these drugs. When initiating therapy, Risperidone tablets should be titrated slowly. It may be necessary to increase the Risperidone tablet dose when enzyme inhibitors such as fluoxetine or paroxetine are discontinued [see Drug Interactions (7.1)].

When Risperidone tablets are coadministered with enzyme inducers (e.g., carbamazepine), the dose of Risperidone tablets should be increased up to double the patient's usual dose. It may be necessary to decrease the Risperidone tablets dose when enzyme inducers such as carbamazepine are discontinued [see Drug Interactions (7.1)]. Similar effect may be expected with coadministration of Risperidone tablets with other enzyme inducers (e.g., phenytoin, rifampin, and phenobarbital).

For patients with severe renal impairment (CLcr < 30 mL/min) or hepatic impairment (10 to 15 points on Child Pugh System), the initial starting dose is 0.5 mg twice daily. The dose may be increased in increments of 0.5 mg or less, administered twice daily. For doses above 1.5 mg twice daily, increase in intervals of one week or greater [see Use in Specific Populations (8.6 and 8.7)].

Patients experiencing persistent somnolence may benefit from a once-daily dose administered at bedtime or administering half the daily dose twice daily, or a reduction of the dose.

Once sufficient clinical response has been achieved and maintained, consider gradually lowering the dose to achieve the optimal balance of efficacy and safety. The physician who elects to use Risperidone tablets for extended periods should periodically re-evaluate the long-term risks and benefits of the drug for the individual patient.

For patients with body weight less than 20 kg, initiate dosing at 0.25 mg per day. For patients with body weight greater than or equal to 20 kg, initiate dosing at 0.5 mg per day. After a minimum of four days, the dose may be increased to the recommended dose of 0.5 mg per day for patients less than 20 kg and 1.0 mg per day for patients greater than or equal to 20 kg. Maintain this dose for a minimum of 14 days. In patients not achieving sufficient clinical response, the dose may be increased at intervals of 2 weeks or greater, in increments of 0.25 mg per day for patients less than 20 kg, or increments of 0.5 mg per day for patients greater than or equal to 20 kg. The effective dose range is 0.5 mg to 3 mg per day. No dosing data are available for children who weigh less than 15 kg.

The dosage of Risperidone tablets should be individualized according to the response and tolerability of the patient. The total daily dose of Risperidone tablets can be administered once daily, or half the total daily dose can be administered twice daily.

There is no body of evidence available from controlled trials to guide a clinician in the longer-term management of a patient who improves during treatment of an acute manic episode with Risperidone tablets. While it is generally agreed that pharmacological treatment beyond an acute response in mania is desirable, both for maintenance of the initial response and for prevention of new manic episodes, there are no systematically obtained data to support the use of Risperidone tablets in such longer-term treatment (i.e., beyond 3 weeks). The physician who elects to use Risperidone tablets for extended periods should periodically re-evaluate the long-term risks and benefits of the drug for the individual patient.

The initial dose is 0.5 mg once daily, administered as a single-daily dose in the morning or evening. The dose may be adjusted at intervals of 24 hours or greater, in increments of 0.5 mg or 1 mg per day, as tolerated, to the recommended target dose of 1 mg to 2.5 mg per day. Although efficacy has been demonstrated in studies of pediatric patients with bipolar mania at doses between 0.5 mg and 6 mg per day, no additional benefit was observed above 2.5 mg per day, and higher doses were associated with more adverse events. Doses higher than 6 mg per day have not been studied.

The initial dose range is 2 mg to 3 mg per day. The dose may be adjusted at intervals of 24 hours or greater, in increments of 1 mg per day. The effective dose range is 1 mg to 6 mg per day, as studied in the short-term, placebo-controlled trials. In these trials, short-term (3 week) anti-manic efficacy was demonstrated in a flexible dosage range of 1 mg to 6 mg per day [see Clinical Studies (14.2 , 14.3)]. Risperidone tablet doses higher than 6 mg per day were not studied.

There are no systematically collected data to specifically address switching schizophrenic patients from other antipsychotics to Risperidone tablets, or treating patients with concomitant antipsychotics.

Although there are no data to specifically address reinitiation of treatment, it is recommended that after an interval off Risperidone tablets, the initial titration schedule should be followed.

While it is unknown how long a patient with schizophrenia should remain on Risperidone tablets, the effectiveness of Risperidone tablets 2 mg per day to 8 mg per day at delaying relapse was demonstrated in a controlled trial in adult patients who had been clinically stable for at least 4 weeks and were then followed for a period of 1 to 2 years [see Clinical Studies (14.1)]. Both adult and adolescent patients who respond acutely should generally be maintained on their effective dose beyond the acute episode. Patients should be periodically reassessed to determine the need for maintenance treatment.

The initial dose is 0.5 mg once daily, administered as a single-daily dose in the morning or evening. The dose may be adjusted at intervals of 24 hours or greater, in increments of 0.5 mg or 1 mg per day, as tolerated, to a recommended dose of 3 mg per day. Although efficacy has been demonstrated in studies of adolescent patients with schizophrenia at doses between 1 mg to 6 mg per day, no additional benefit was observed above 3 mg per day, and higher doses were associated with more adverse events. Doses higher than 6 mg per day have not been studied.

Risperidone tablets can be administered once or twice daily. Initial dosing is 2 mg per day. May increase the dose at intervals of 24 hours or greater, in increments of 1 to 2 mg per day, as tolerated, to a recommended dose of 4 to 8 mg per day. In some patients, slower titration may be appropriate. Efficacy has been demonstrated in a range of 4 mg to 16 mg per day. However, doses above 6 mg per day for twice daily dosing were not demonstrated to be more efficacious than lower doses, were associated with more extrapyramidal symptoms and other adverse effects, and are generally not recommended. In a single study supporting once-daily dosing, the efficacy results were generally stronger for 8 mg than for 4 mg. The safety of doses above 16 mg per day has not been evaluated in clinical trials [see Clinical Studies (14.1)].

Severe Renal and Hepatic Impairment in Adults: use a lower starting dose of 0.5 mg twice daily. May increase to dosages above 1.5 mg twice daily at intervals of one week or longer.

Risperidone tablets are available in the following strengths and colors: 0.25 mg (dark-yellow), 0.5 mg (red-brown), 1 mg (white to off-white), 2 mg (orange), 3 mg (yellow), and 4 mg (green). All are debossed with “93” on one side and either “221”, “225”, “7240”, “7241”, “7242”, or “7243” on the other side according to their respective strengths.

Risperidone tablets are contraindicated in patients with a known hypersensitivity to Risperidone tablets. Hypersensitivity reactions, including anaphylactic reactions and angioedema, have been observed in patients treated with Risperidone.

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10 week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. In two of four placebo-controlled trials in elderly patients with dementia-related psychosis, a higher incidence of mortality was observed in patients treated with furosemide plus Risperidone when compared to patients treated with Risperidone alone or with placebo plus furosemide. No pathological mechanism has been identified to explain this finding, and no consistent pattern for cause of death was observed. Risperidone is not approved for the treatment of dementia-related psychosis [see Boxed Warning].

Antipsychotic drugs including Risperidone can cause a potentially fatal symptom complex referred to as Neuroleptic Malignant Syndrome (NMS). Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered mental status, and autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase (CPK), myoglobinuria, rhabdomyolysis, and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases in which the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology. The management of NMS should include: (1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; (2) intensive symptomatic treatment and medical monitoring; and (3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, prescribe Risperidone in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that: (1) is known to respond to antipsychotic drugs, and (2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient treated with Risperidone, consider drug discontinuation. However, some patients may require treatment with Risperidone despite the presence of the syndrome.

Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include hyperglycemia, dyslipidemia, and body weight gain. While all of the drugs in the class have been shown to produce some metabolic changes, each drug has its own specific risk profile. Hyperglycemia and diabetes mellitus, in some cases

extreme and associated with ketoacidosis or hyperosmolar coma or death, have been reported in patients treated with atypical antipsychotics including Risperidone. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics, including Risperidone, should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics, including Risperidone, should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics, including Risperidone, should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics, including Risperidone, should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic, including Risperidone, was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of Risperidone. Pooled data from three double-blind, placebo-controlled schizophrenia studies and four double-blind, placebo-controlled bipolar monotherapy studies are presented in Table 2. Table 2. Change in Random Glucose From Seven Placebo-Controlled, 3 to 8 Week, Fixed- or Flexible-Dose Studies in Adult Subjects With Schizophrenia or Bipolar Mania In longer-term, controlled and uncontrolled studies, Risperidone was associated with a mean change in glucose of +2.8 mg/dL at Week 24 (n = 151) and +4.1 mg/dL at Week 48 (n = 50). Data from the placebo-controlled 3 to 6 week study in children and adolescents with schizophrenia (13 to 17 years of age), bipolar mania (10 to 17 years of age), or autistic disorder (5 to 17 years of age) are presented in Table 3. Table 3. Change in Fasting Glucose From Three Placebo-Controlled, 3 to 6 Week, Fixed-Dose Studies in Children and Adolescents With Schizophrenia (13 to 17 Years of Age), Bipolar Mania (10 to 17 Years of Age), or Autistic Disorder (5 to 17 Years of Age) In longer-term, uncontrolled, open-label extension pediatric studies, Risperidone was associated with a mean change in fasting glucose of +5.2 mg/dL at Week 24 (n = 119). Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics. Pooled data from 7 placebo-controlled, 3 to 8 week, fixed- or flexible-dose studies in adult subjects with schizophrenia or bipolar mania are presented in Table 4. Table 4. Change in Random Lipids From Seven Placebo-Controlled, 3 to 8 Week, Fixed- or Flexible-Dose Studies in Adult Subjects With Schizophrenia or Bipolar Mania In longer-term, controlled and uncontrolled studies, Risperidone was associated with a mean change in (a) non-fasting cholesterol of +4.4 mg/dL at Week 24 (n = 231) and +5.5 mg/dL at Week 48 (n = 86); and (b) non-fasting triglycerides of +19.9 mg/dL at Week 24 (n = 52). Pooled data from 3 placebo-controlled, 3 to 6 week, fixed-dose studies in children and adolescents with schizophrenia (13 to 17 years of age), bipolar mania (10 to 17 years of age), or autistic disorder (5 to 17 years of age) are presented in Table 5. Table 5. Change in Fasting Lipids From Three Placebo-Controlled, 3 to 6 Week, Fixed-Dose Studies in Children and Adolescents With Schizophrenia (13 to 17 Years of Age), Bipolar Mania (10 to 17 Years of Age), or Autistic Disorder (5 to 17 Years of Age) In longer-term, uncontrolled, open-label extension pediatric studies, Risperidone was associated with a mean change in (a) fasting cholesterol of +2.1 mg/dL at Week 24 (n = 114); (b) fasting LDL of -0.2 mg/dL at Week 24 (n = 103); (c) fasting HDL of +0.4 mg/dL at Week 24 (n = 103); and (d) fasting triglycerides of +6.8 mg/dL at Week 24 (n = 120). Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended. Data on mean changes in body weight and the proportion of subjects meeting a weight gain criterion of 7% or greater of body weight from 7 placebo-controlled, 3 to 8 week, fixed- or flexible-dose studies in adult subjects with schizophrenia or bipolar mania are presented in Table 6. Table 6. Mean Change in Body Weight (kg) and the Proportion of Subjects With ≥ 7% Gain in Body Weight From Seven Placebo-Controlled, 3 to 8 Week, Fixed- or Flexible-Dose Studies in Adult Subjects With Schizophrenia or Bipolar Mania In longer-term, controlled and uncontrolled studies, Risperidone was associated with a mean change in weight of +4.3 kg at Week 24 (n = 395) and +5.3 kg at Week 48 (n = 203). Data on mean changes in body weight and the proportion of subjects meeting the criterion of ≥ 7% gain in body weight from nine placebo-controlled, 3 to 8 week, fixed-dose studies in children and adolescents with schizophrenia (13 to 17 years of age), bipolar mania (10 to 17 years of age), autistic disorder (5 to 17 years of age), or other psychiatric disorders (5 to 17 years of age) are presented in Table 7. Table 7. Mean Change in Body Weight (kg) and the Proportion of Subjects With ≥ 7% Gain in Body Weight From Nine Placebo-Controlled, 3 to 8 Week, Fixed-Dose Studies in Children and Adolescents With Schizophrenia (13 to 17 Years of Age), Bipolar Mania (10 to 17 Years of Age),

Autistic Disorder (5 to 17 Years of Age) or Other Psychiatric Disorders (5 to 17 Years of Age) In longer-term, uncontrolled, open-label extension pediatric studies, Risperidone was associated with a mean change in weight of +5.5 kg at Week 24 (n = 748) and +8.0 kg at Week 48 (n = 242). In a long-term, open-label extension study in adolescent patients with schizophrenia, weight increase was reported as a treatment-emergent adverse event in 14% of patients. In 103 adolescent patients with schizophrenia, a mean increase of 9.0 kg was observed after 8 months of Risperidone treatment. The majority of that increase was observed within the first 6 months. The average percentiles at baseline and 8 months, respectively, were 56 and 72 for weight, 55 and 58 for height, and 51 and 71 for body mass index. In long-term, open-label trials (studies in patients with autistic disorder or other psychiatric disorders), a mean increase of 7.5 kg after 12 months of Risperidone treatment was observed, which was higher than the expected normal weight gain (approximately 3 to 3.5 kg per year adjusted for age, based on Centers for Disease Control and Prevention normative data). The majority of that increase occurred within the first 6 months of exposure to Risperidone. The average percentiles at baseline and 12 months, respectively, were 49 and 60 for weight, 48 and 53 for height, and 50 and 62 for body mass index. In one 3 week, placebo-controlled trial in children and adolescent patients with acute manic or mixed episodes of bipolar I disorder, increases in body weight were higher in the Risperidone groups than the placebo group, but not dose related (1.90 kg in the Risperidone 0.5 to 2.5 mg group, 1.44 kg in the Risperidone 3 to 6 mg group, and 0.65 kg in the placebo group). A similar trend was observed in the mean change from baseline in body mass index. When treating pediatric patients with Risperidone for any indication, weight gain should be assessed against that expected with normal growth.

As with other drugs that antagonize dopamine D2 receptors, Risperidone elevates prolactin levels and the elevation persists during chronic administration. Risperidone is associated with higher levels of prolactin elevation than other antipsychotic agents. Hyperprolactinemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotropin secretion. This, in turn, may inhibit reproductive function by impairing gonadal steroidogenesis in both female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds. Long-standing hyperprolactinemia when associated with hypogonadism may lead to decreased bone density in both female and male subjects. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in a patient with previously detected breast cancer. An increase in pituitary gland, mammary gland, and pancreatic islet cell neoplasia (mammary adenocarcinomas, pituitary and pancreatic adenomas) was observed in the Risperidone carcinogenicity studies conducted in mice and rats [see Nonclinical Toxicology (13.1)]. Neither clinical studies nor epidemiologic studies conducted to date have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is considered too limited to be conclusive at this time.

Risperidone may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period, probably reflecting its alpha-adrenergic antagonistic properties. Syncope was reported in 0.2% (6/2607) of Risperidone-treated patients in Phase 2 and 3 studies in adults with schizophrenia. The risk of orthostatic hypotension and syncope may be minimized by limiting the initial dose to 2 mg total (either once daily or 1 mg twice daily) in normal adults and 0.5 mg twice daily in the elderly and patients with renal or hepatic impairment [see Dosage and Administration (2.1, 2.4)]. Monitoring of orthostatic vital signs should be considered in patients for whom this is of concern. A dose reduction should be considered if hypotension occurs. Risperidone should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, and conditions which would predispose patients to hypotension, e.g., dehydration and hypovolemia. Clinically significant hypotension has been observed with concomitant use of Risperidone and antihypertensive medication.

Class Effect: In clinical trial and/or postmarketing experience, events of leukopenia/neutropenia have been reported temporally related to antipsychotic agents, including Risperidone. Agranulocytosis has also been reported. Possible risk factors for leukopenia/neutropenia include preexisting low white blood cell count (WBC) and history of drug-induced leukopenia/neutropenia. Patients with a history of a clinically significant low WBC or a drug-induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and discontinuation of Risperidone should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors. Patients with clinically significant neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count < 1000/mm3) should

discontinue Risperidone and have their WBC followed until recovery.

Somnolence was a commonly reported adverse reaction associated with Risperidone treatment, especially when ascertained by direct questioning of patients. This adverse reaction is dose-related, and in a study utilizing a checklist to detect adverse events, 41% of the high-dose patients (Risperidone 16 mg/day) reported somnolence compared to 16% of placebo patients. Direct questioning is more sensitive for detecting adverse events than spontaneous reporting, by which 8% of Risperidone 16 mg/day patients and 1% of placebo patients reported somnolence as an adverse reaction. Since Risperidone has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Risperidone therapy does not affect them adversely.

risperidone oral : Uses, Side Effects, Interactions, Pictures, Warnings & Dosing

http://www.webmd.com/drugs/2/drug-6283-2034/risperidone-oral/risperidone-oral/details December 09, 2014

Find patient medical information for risperidone oral on WebMD including its uses, side effects and safety, interactions, pictures, warnings and user ratings.

Before taking risperidone, tell your doctor or pharmacist if you are allergic to it; or to paliperidone; or if you have any other allergies. This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to your pharmacist for more details.

Before using this medication, tell your doctor or pharmacist your medical history, especially of: liver disease, kidney disease, seizures, difficulty swallowing, low white blood cell count, Parkinson's disease, dementia, certain eye problems (cataracts, glaucoma).

Also tell your doctor or pharmacist if either you or a family member has a history of the following: diabetes, heart disease, high blood cholesterol/triglyceride levels, high blood pressure, obesity.

Risperidone may cause a condition that affects the heart rhythm (QT prolongation). QT prolongation can infrequently result in serious (rarely fatal) fast/irregular heartbeat and other symptoms (such as severe dizziness, fainting) that need medical attention right away.

The risk of QT prolongation may be increased if you have certain medical conditions or are taking other drugs that may cause QT prolongation. Before using risperidone, tell your doctor or pharmacist of all the drugs you take and if you have any of the following conditions: certain heart problems (heart failure, slow heartbeat, QT prolongation in the EKG), family history of certain heart problems (QT prolongation in the EKG, sudden cardiac death).

Low levels of potassium or magnesium in the blood may also increase your risk of QT prolongation. This risk may increase if you use certain drugs (such as diuretics/"water pills") or if you have conditions such as severe sweating, diarrhea, or vomiting. Talk to your doctor about using risperidone safely.

This drug may make you dizzy or drowsy. Do not drive, use machinery, or do any activity that requires alertness until you are sure you can perform such activities safely. Avoid alcoholic beverages.

Before having surgery (including cataract/glaucoma eye surgery), tell your doctor or dentist if you are taking or have ever taken this medication, and about all the other products you use (including prescription drugs, nonprescription drugs, and herbal products).

This medication may make you sweat less, making you more likely to get heat stroke. Avoid doing things that may cause you to overheat, such as hard work or exercise in hot weather, or using hot tubs. When the weather is hot, drink a lot of fluids and dress lightly. If you overheat, quickly look for a place to cool down and rest. Get medical help right away if you have a fever that does not go away, mental/mood changes, headache, or dizziness.

Older adults may be more sensitive to the side effects of this drug, especially dizziness, lightheadedness, and QT prolongation (see above).

During pregnancy, this medication should be used only when clearly needed. Discuss the risks and benefits with your doctor. Do not stop taking this medication unless directed by your doctor. Babies born to mothers who have used this drug during the last 3 months of pregnancy may infrequently develop symptoms including muscle stiffness or shakiness, drowsiness, feeding/breathing difficulties, or

constant crying. If you notice any of these symptoms in your newborn anytime during their first month, tell the doctor right away.

This medication passes into breast milk and may have undesirable effects on a nursing infant. Consult your doctor before breast-feeding.

Risperdal (Risperidone) Drug Information: Description, User Reviews, Drug Side Effects, Interactions

http://www.rxlist.com/risperdal-drug.htm December 09, 2014

Learn about the prescription medication Risperdal (Risperidone), drug uses, dosage, side effects, drug interactions, warnings, reviews and patient labeling.

RISPERDAL® contains risperidone, an atypical antipsychotic belonging to the chemical class of benzisoxazole derivatives. The chemical designation is 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one. Its molecular formula is C H FN O and its molecular weight is 410.49. The structural formula is:

Risperidone is a white to slightly beige powder. It is practically insoluble in water, freely soluble in methylene chloride, and soluble in methanol and 0.1 N HCl.

RISPERDAL® Tablets are for oral administration and available in 0.25 mg (dark yellow), 0.5 mg (red-brown), 1 mg (white), 2 mg (orange), 3 mg (yellow), and 4 mg (green) strengths. RISPERDAL® tablets contain the following inactive ingredients: colloidal silicon dioxide, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol, sodium lauryl sulfate, and starch (corn). The 0.25 mg, 0.5 mg, 2 mg, 3 mg, and 4 mg tablets also contain talc and titanium dioxide. The 0.25 mg tablets contain yellow iron oxide; the 0.5 mg tablets contain red iron oxide; the 2 mg tablets contain FD&C Yellow No. 6 Aluminum Lake; the 3 mg and 4 mg tablets contain D&C Yellow No. 10; the 4 mg tablets contain FD&C Blue No. 2 Aluminum Lake.

RISPERDAL® is also available as a 1 mg/mL oral solution. RISPERDAL® Oral Solution contains the following inactive ingredients: tartaric acid, benzoic acid, sodium hydroxide, and purified water.

RISPERDAL® M-TAB® Orally Disintegrating Tablets are available in 0.5 mg (light coral), 1 mg (light coral), 2 mg (coral), 3 mg (coral), and 4 mg (coral) strengths. RISPERDAL® M-TAB® Orally Disintegrating Tablets contain the following inactive ingredients: Amberlite® resin, gelatin, mannitol, glycine, simethicone, carbomer, sodium hydroxide, aspartame, red ferric oxide, and peppermint oil. In addition, the 2 mg, 3 mg, and 4 mg RISPERDAL® M-TAB® Orally Disintegrating Tablets contain xanthan gum.

What are the possible side effects of risperidone (Risperdal, Risperdal M-Tab)? Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficulty breathing; swelling of your face, lips, tongue, or throat. Stop taking risperidone and call your doctor at once if you have a serious side effect such as: restless muscle movements in your eyes, tongue, jaw, or neck; Read All Potential Side Effects and See Pictures of Risperdal » What are the precautions when taking risperidone (Risperdal)? Before taking risperidone, tell your doctor or pharmacist if you are allergic to it; or to paliperidone; or if you have any other allergies. This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to your pharmacist for more details. Before using this medication, tell your doctor or pharmacist your medical history, especially of: liver disease, kidney disease, seizures, difficulty swallowing, low white blood cell count, Parkinson's disease, dementia. Also tell your doctor or pharmacist if either you or a family member has a history of the following: diabetes, heart disease, high blood cholesterol/triglyceride levels, high blood pressure, obesity. Risperidone may cause a condition that affects the heart rhythm (QT...

Last reviewed on RxList: 5/8/2014

This monograph has been modified to include the generic and brand name in many instances.

definition of risperidone by Medical dictionary

http://medical-dictionary.thefreedictionary.com/risperidone December 09, 2014

risperidone. Risperdal, Risperdal Consta, Risperdal M-Tab. Pharmacologic class: Benzisoxazole derivative. Therapeutic class: Antipsychotic. Pregnancy risk category C.

/ris·per·i·done/ ( ) an n. A dopamine and serotonin antagonist used to treat the hallucinations, delusions, and thought disturbances of schizophrenia and other psychoses. [ ] an orally administered; its mechanism of action is unknown, but it may function as an antagonist to dopamine and serotonin n brand name: Risperdal;

drug class: antipsychotic;

action: may be related to antagonism for dopamine and serotonin receptors; also has affinity for alpha receptors and histamine (H) receptors;

use: psychotic disorders. • Elderly patients with dementia-related psychosis are at increased risk for death. Over course of 10-week controlled trial, death rate in drug-treated patients was about 4.5%, compared to about 2.6% in placebo group. Although causes of death varied, most appeared to be cardiovascular or infectious. Don't give drug to patients with dementia-related psychosis. Antagonizes serotonin and dopamine receptors in CNS. Also binds to alpha - and alpha -adrenergic receptors and histamine H receptors. Powder for injection (extended release): 25-mg, 37.5-mg, 50-mg vials in dose pack with diluent in prefilled syringes Adults: 1 mg P.O. b.i.d., increased by 1 mg b.i.d. as tolerated on days 2 and 3, up to a target dosage of 3 mg b.i.d. by day 3. May adjust in increments or decrements of 1 mg b.i.d. at weekly intervals; usual dosage range is 4 to 8 mg/day. Alternatively, may give as a single daily dose after initial titration. Or 25 mg deep I.M. q 2 weeks. Maximum dosage is 50 mg q 2 weeks. Adolescents ages 13 to17: 0.5 mg P.O. as single daily dose in morning or evening. Dosage adjustments, if indicated, should occur at intervals of not less than 24 hours, in increments of 0.5 or 1 mg/day, as tolerated, to recommended dosage of 3 mg/day. Adults: Initially, 2 to 3 mg/day P.O. May adjust in increments or decrements of 1 mg/day at 24-hour intervals. Range is 1 to 6 mg/day. Children: 0.5 mg P.O. as single daily dose in morning or evening. Dosage adjustments, if indicated, should occur at intervals of not less than 24 hours, in increments of 0.5 or 1 mg/day, as tolerated, to recommended dosage of 2.5 mg/day. Irritability symptoms of aggression toward others, deliberate self-injury, and temper tantrums associated with autistic disorder Adolescents and children: Initially, 0.25 mg P.O. (Risperdal) daily for patients weighing less than 20 kg (44 lb) and 0.5 mg/day for patients weighing 20 kg or more. After minimum of 4 days, increase as needed to recommended dosage of 0.5 mg/day for patients weighing less than 20 kg and 1 mg/day for patients weighing 20 kg or more. Maintain this dosage for minimum of 14 days. If sufficient clinical response not achieved, consider dosage increases at 2-week or more intervals in increments of 0.25 mg/day for patients weighing less than 20 kg or 0.5 mg/day for patients weighing 20 kg or more. Once sufficient clinical response has been achieved and maintained, consider gradually lowering dosage to achieve optimal balance of efficacy and safety. Use cautiously in:

• renal or hepatic impairment, cardiovascular disease, prolonged QT interval, dysphagia, hyperprolactinemia, hypothermia or hyperthermia, Parkinson's disease, phenylketonuria, tardive dyskinesia, previous diagnosis of breast cancer or prolactin-dependent tumors

• history of seizures, drug abuse, or suicide attempt

• elderly or debilitated patients

• pregnant patients

• breastfeeding patients (use not recommended)

• children (safety not established for Risperdal Consta, Risperdal M-Tab, and Risperdal in children weighing less than 33 lb [15 kg]). Do not give powder for injection I.V.

• When reconstituting powder for injection, use only the diluent and needle supplied.

• Shake vial vigorously for a minimum of 10 seconds to ensure homogeneous suspension. When properly mixed, the suspension appears uniform, thick, and milky with visible particles.

• If 2 minutes elapse before giving injection, shake vial vigorously before administering. Give injection within 6 hours of reconstitution.

• Record baseline blood pressure before starting therapy.

• For I.M. use, inject deep into buttock; rotate injection sites between buttocks.

• Be aware that children and adolescents experiencing persistent somnolence may benefit from once-daily Risperdal dose administered at bedtime, from administering half daily dose twice daily, or from reduction of dose. Levodopa, other dopamine agonists: decreased antiparkinsonian effects of these drugs Closely monitor neurologic status, especially for neuroleptic malignant syndrome (high fever, sweating, unstable blood pressure, stupor, muscle rigidity, and autonomic dysfunction), extrapyramidal reactions, TIA, CVA, and tardive dyskinesia.

• Monitor blood pressure, particularly for orthostatic hypotension.

• Assess body temperature. Check for fever and other signs and symptoms of infection. • Instruct patient to remove orally disintegrating tablet from blister pack, place on tongue immediately, and swallow as tablet dissolves.

• Tell patient to mix oral solution with water, coffee, orange juice, or low-fat milk. Tell him solution isn't compatible with cola or tea.

• Advise patient to use effective bedtime routine to avoid sleep disorders.

Teach patient to recognize and immediately report signs and symptoms of serious adverse reactions, including tardive dyskinesia and neuroleptic malignant syndrome.

• Instruct patient to move slowly when sitting up or standing, to avoid dizziness from sudden blood pressure decrease.

• Tell patient that excessive fluid loss (as from sweating, vomiting, or diarrhea) and inadequate fluid intake increase risk of light-headedness (especially in hot weather).

• Caution patient to avoid driving and other hazardous activities until he knows how drug affects concentration and alertness.

• Advise female patient to tell prescriber if she is or plans to become pregnant. Caution her not to breastfeed during therapy.

• Advise patient not to drink alcohol.

• As appropriate, review all other significant and life-threatening adverse reactions and interactions, especially those related to the drugs and behaviors mentioned above. /ris·per·i·done/ () an antipsychotic agent, which may act by a combination of dopamine and serotonin antagonism.

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Risperidone - Risperdal

http://www.patient.co.uk/medicine/risperidone-risperdal December 09, 2014

Risperidone is prescribed for a variety of problems affecting thoughts, feelings or behaviours. Ask your doctor if you are unsure why it has been prescribed for you.

Risperidone is prescribed for a variety of problems affecting thoughts, feelings or behaviours. Ask your doctor if you are unsure why it has been prescribed for you.

Risperidone belongs to a group of medicines called antipsychotics. These medicines work on the balance of chemical substances in the brain.

You may have been prescribed risperidone to relieve the symptoms of schizophrenia or a similar mental health problem affecting your thoughts, feelings or behaviours. These problems are called psychoses. It is also given to treat aggressive behaviour problems in some people where these could become a danger to self or to others.

Risperidone can also be given by injection and there is a separate medicine leaflet for this called Risperidone long-acting injection.

Some medicines are not suitable for people with certain conditions, and sometimes a medicine may only

be used if extra care is taken. For these reasons, before you start taking risperidone it is important that your doctor knows:

Along with their useful effects, most medicines can cause unwanted side-effects although not everyone experiences them. The table below contains some of the most common ones associated with risperidone. You will find a full list in the manufacturer's information leaflet supplied with your medicine. The unwanted effects often improve as your body adjusts to the new medicine, but speak with your doctor or pharmacist if any of the following continue or become troublesome.

Important: if you experience symptoms such as muscle stiffness, a very high temperature, feeling confused, a fast heartbeat and sweating, you should contact your doctor immediately. These can be signs of a rare but serious condition known as neuroleptic malignant syndrome.

If you experience any other symptoms which you think may be due to the medicine, speak with your doctor or pharmacist for further advice.

dose, effects, therapy, adults, drug, people, used, brain

http://www.minddisorders.com/Py-Z/Risperidone.html December 09, 2014

Risperidone is an atypical antipsychotic agent for two reasons. First, it is chemically unrelated to the older antipsychotic drugs. Second, unlike older ...

Risperidone is an atypical antipsychotic agent for two reasons. First, it is chemically unrelated to the older antipsychotic drugs. Second, unlike older antipsychotic drugs that primarily inhibit the actions of dopamine, a chemical in the brain , risperidone may also have some action against another brain chemical, serotonin. The proper level of both dopamine and serotonin are influential in maintaining mental well-being. An advantage of using risperidone over one of the older antipsychotic drugs is a lower incidence of parkinsonian-like side effects. These side effects may be sufficiently troublesome to cause patients to discontinue treatment for their schizophrenia. For this reason, patients who have had negative experiences with older antipsychotics may benefit from risperidone. Also, some patients who showed little improvement with older antipsychotic drugs respond better to risperidone. Risperidone is available in 0.25-mg, 0.5-mg, 1-mg, 2-mg, 3-mg, and 4-mg tablets and a solution containing 1 mg of drug in each milliliter of solution.

For treating psychotic disorders in adults, the usual starting dose of risperidone is 1 mg twice daily. Dosage is increased gradually until a target dose of 3 mg twice daily is reached. Some patients do just as well with a single daily dose (6 mg once a day, for example). There is little clinical evidence to indicate that increasing the daily dose beyond 8 mg offers additional benefit. However, higher doses may contribute to additional side effects. If the dose needs to be adjusted, the changes should made no more often than once per week. In older patients (over age 60), starting dosage should not exceed 1 mg daily. Most patients should not take more than 3 mg daily. People with low blood pressure and those who have kidney disease should take a similarly reduced dose.

Patients with a history of cardiovascular disease or low blood pressure should take risperidone only after discussing the risks and benefits with their physician, and then with close physician monitoring. Risperidone has occasionally been associated with seizures . People with a past history of seizures should discuss with their doctor whether risperidone is the right antipsychotic for them to use. People taking risperidone should avoid operating a motor vehicle or other dangerous machinery until they see how risperidone affects them. Some people have trouble regulating their body temperature while taking risperidone. Patients receiving this drug should be aware of this and avoid extremes in outdoor temperatures.

The most common and bothersome side effect associated with risperidone is decreased blood pressure while standing up (known as orthostatic hypotension). This can cause dizziness or fainting. A decrease in blood pressure usually occurs early in therapy, while the proper dose is being established. It is more common in older patients than in younger ones. Usually, this side effect disappears entirely with time. If it continues, the physician may decrease the dose. Meanwhile, people taking risperidone should be aware of this side effect and get up slowly if they have been sitting for an extended time. The most common nervous system side effects of risperidone include insomnia , agitation, anxiety, and headache. Early in therapy, patients may experience an inability to think clearly or perform certain tasks that require mental alertness. High doses of risperidone can cause unwanted sleepiness in about 40% of patients. Antipsychotic drugs, including risperidone, can cause side effects that are similar to the symptoms of

Parkinson's disease. The patient does not have Parkinson's disease, but may have shaking in muscles at rest, difficulty with voluntary movements, and poor muscle tone. These symptoms normally disappear if the drug is stopped. The most common gastrointestinal side effects include nausea, vomiting, constipation, and difficulty digesting food. Up to 10% of patients taking risperidone experience rhinitis (runny nose).

There is very little information about how risperidone interacts with other drugs. However, because some patients receiving risperidone experience lowered blood pressure while standing, it is expected that other drugs that lower blood pressure may increase the incidence and severity of this side effect when taken with risperidone.

risperidone

http://www.pharmgkb.org/drug/PA451257 December 09, 2014

Dutch Pharmacogenetics Working Group Guideline for risperidone and CYP2D6 Summary. Select an alternative drug or be extra alert to adverse drug events ...

Risperidone is metabolized to 9-hydroxyrisperidone by CYP2D6. Co-administration of drugs that are inhibitors or inducers of CYP2D6 along with risperidone may alter the plasma concentration of risperidone.

Risperidone is an atypical antipsychotic used in the treatment of schizophrenia, bipolar I disorder, and autism. CYP2D6 is important in its metabolism.

Risperidone is metabolized to 9-hydroxyrisperidone by CYP2D6, an enzyme that is polymorphic in the population and that can be inhibited by a variety of psychotropic and other drugs (see Clinical Pharmacology (12.3)). Drug interactions that reduce the metabolism of risperidone to 9-hydroxyrisperidone would increase the plasma concentrations of risperidone and lower the concentrations of 9-hydroxyrisperidone. Analysis of clinical studies involving a modest number of poor metabolizers does not suggest that poor and extensive metabolizers have different rates of adverse effects. No comparison of effectiveness in the two groups has been made.

CYP2D6 is subject to genetic polymorphism (about 6% to 8% of Caucasians, and a very low percentage of Asians, have little or no activity and are "poor metabolizers") and to inhibition by a variety of substrates and some non-substrates, notably quinidine. Extensive CYP2D6 metabolizers convert risperidone rapidly into 9-hydroxyrisperidone, whereas poor CYP2D6 metabolizers convert it much more slowly. Although extensive metabolizers have lower risperidone and higher 9- hydroxyrisperidone concentrations than poor metabolizers, the pharmacokinetics of risperidone and 9-hydroxyrisperidone combined, after single and multiple doses, are similar in extensive and poor metabolizers.

For the complete drug label text with sections containing pharmacogenetic information highlighted, see the Risperidone drug label.

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Focus on the antipsychotic

http://www.priory.com/focus9.htm December 09, 2014

Keywords: Schizophrenia - risperidone - antipsychotic - neuroleptic - atypical - pharmacology . Summary. Risperidone is a relatively new antipsychotic available world ...

Risperidone is a relatively new antipsychotic available world-wide since the early 1990s. It has been characterised as atypical, but shares some of the extrapyramidal side effect profile of the earlier antipsychotics, particularly at higher doses.

Risperidone has been developed by Janssen-Cilag. It is a novel antipsychotic with dopaminergic and serotonergic effects. Risperidone is available in tablet and liquid form. A depot formulation is available (Risperdal Consta®).

The main pharmacological activities of risperidone include serotonin 5-HT2 receptor blockade and dopamine D2 antagonism (Megens et al, 1994). After oral administration of 1 mg of risperidone 5-HT2

receptor occupancy is about 60% and D2 dopamine receptor occupancy in the striatum is about 50% (Nyberg et al, 1993). In common with other antipsychotics, risperidone enhances prolactin release, but some central effects such as catalepsy and blockade of motor activity occur at high doses only. Risperidone is 4-10 times less potent than the conventional antipsychotic haloperidol as a central D2 antagonist in rats. Interaction with dopamine D1 receptors occurs only at very high concentrations. The pharmacological profile of risperidone includes interaction with histamine H1 and alpha-adrenergic receptors but the compound does not interact significantly with cholinergic receptors.The drug has good activity against various symptoms and signs associated with schizophrenia (Marder, Davis & Chouinard, 1997). Compared to conventional antipsychotics such as haloperidol risperidone produces some significantly better results according to Positive and Negative Syndrome Scale (PANSS) scores. Marder et al's study (1997) factor analysed the PANSS scores and produced five dimensions; negative symptoms, positive symptoms, disorganized thought, uncontrolled hostility/excitement, and anxiety/depression. The study looked at 513 patients intwo double-blind trials. Symptom reductions in PANSS factor scores from baseline to treatment at weeks 6 and 8 were significantly greater in patients receiving 6-16 mg/day of risperidone than in patients receiving placebo or haloperidol.The advantages of risperidone were greatest for negative symptoms, uncontrolled hostility/excitement, and anxiety/depression.

Meta-analysis from available randomised, double-masked, comparative trials of risperidone and haloperidol in patients with schizophrenia treated for at least 4 weeks at recommended doses (Davies et al, 1998). Six out of nine trials met all criteria for inclusion in the meta-analysis which showed that in patients with chronic schizophrenia, risperidone therapy is associated with significantly higher response rates, significantly less prescribing of anticholinergic medication, and significantly lower treatment dropout rates than haloperidol.

The drug is available in 0.25, 0.5, 1, 2, 3 and 4 mg tablets.

In adults the suggested initial dose schedule for risperidone is to titrate doses upward from 1 mg twice daily, to 2mg b.d. the next day and 3 mg b.d. the day after to achieve a dose of 4-6mg daily. However, there has been recent work recommending a less rapid titration (over 6 days to a week) and that the dose increments consist of 0.5-2 mg/day (Luchins et al, 1998). The starting dose in the eldelry is 0.5 mg b.d. with 0.5 mg increements to 2 mg b.d.

The conventional dosing regime is twice daily, although there has been recent interest in a once-daily regime. A recent double-blind 6-week study of 211 patients with acute exacerbation were randomly assigned to receive risperidone at 8 mg once daily or 4 mg twice daily. The study demonstrated little clinical difference between 8mg given once daily and 4mg given twice daily (Nair, 1998).In terms of switching patients over from conventional antipsychotics to risperidone about sixty per cent of patients can have their current neuroleptics stopped and risperidone started immediately together with a gradual withdrawal of anticholinergic treatments (Kirov et al, 1997).). This strategy is understandably more successful for who previously received conventional antipsychotics as depot medication.

Nyberg et al (1999) have suggested 4mg/day as the best minimal dosage regime based on PET receptor occupancy studies.They comment that treatment with risperidone, 6 mg/day, is likely to induce unnecessarily high D2 receptor occupancy, with a consequent extrapyramidal side effects. They found that high 5-HT2A receptor occupancy did not prevent extrapyramidal side effects completely. The authors previously suggested an optimal interval for D2 receptor occupancy of 70%-80%. To achieve this, they suggested risperidone, 4 mg/day, as a suitable initial dose for antipsychotic effect with a minimal risk of extrapyramidal side effects in most patients.

It is the Serotonin 5-HT and Dopamine D receptor occupancy that seem to provide the therapeutic effects of risperidone. In vivo PET studies have found that the Serotonin 5-HT and Dopamine D receptor occupancy rates are 60% in the neocortex and 50% in the striatum for the respective receptor types (Nyberg et al, 1993). The Serotonin 5-HT binding in the cortex disinhibits the mesocortical dopamine system , resulting in an increase in dopamine transmission in this pathway and is thought to account for the clinical efficacy against negative and affective symptoms.

Risperidone (R64 766) is a benzisoxazole derivative whose molecular formula is C H FN O Figure One is a diagram of the risperidone molecule.

As far as the manufacturers are concerned risperidone is indicated for acute and chronic schizophrenic psychoses and other psychotic conditions with positive and negative symptoms. It is also indicated for

affective symptoms associated with schizophrenia (ABPI, 1998). There is ample evidence of its efficacy, (Song, 1997).

There is some evidence that risperidone is useful to some extent in reducing aggression in schizophrenia, (Buckley et al, 1997) although possibly not more effectively than typical antipsychotics (Beck et al, 1997).Delusions of infestation appear responsive in small series studies, (De Leon et al, 1997).There is some evidence for its usefulness as an adjunctive therapy in acute bipolar affective disorder in outpatients (Ghaemi et al, 1997) and in bipolar disorder when followed up over a six month period (Ghaemi & Sachs, 1997). It has been postulated that there is dopaminergic mediation as well as a serotonergic mediation for some obsessive and related disorders e.g. Tourette's syndrome. Risperidone has therefore also been used to augment SSRIs in obsessive compulsive disorder (Saxena et al, 1996, Stein et al, 1997). In Saxena et al's study about eighty per cent of patients improved within three weeks of the addition of risperidone. In a series of 22 patients risperidone was found to be effective in 58 %, (Bruun & Budman, 1996). In affective psychoses, risperidone is probably not useful as a single therapeutic agent, that is to say it does not seem to replace an antipsychotic/antidepressant combination (Muller et al, 1998).Risperidone has been found useful in adolescent schizophrenia (Armenteros et al, 1997) and in children with autistic/pervasive developmental disorders (McDougle et al, 1997, Findling et al, 1997).There has been considerable interest and study of its use in the elderly. There has been documented beneficial use in dementia with persistent voacalisations (Kopala & Honer, 1997), and in demented people with Parkinson's (Workman et al, 1997). Katz et al (1999) found that 1 mg/day was useful in controlling aggression in severe dementia.There is ample study and anecdotal evidence for the use of risperidone in liaison psychiatry, uses include delirium (Siphimalani & Masand, 1997, Furmaga et al, 1997), HIV related psychotic disorders (Singh et al, 1997)

Risperidone is rapidly and very well absorbed after administration orally; less than 1% is excreted unchanged in the faeces (Heykants et al, 1994). Risperidone is 90% plasma protein bound (Borison et al, 1994). The principal metabolite is 9-hydroxyrisperidone. Hydroxylation of risperidone is subject to the same genetic CYP2D6-related polymorphism as for debrisoquine and dextromethorphan. In poor metabolizers the half-life of risperidone was about 20 hours compared with about 3 hours in extensive metabolizers (Huang et al, 1993). However, because the pharmacology of 9-hydroxyrisperidone is very similar to that of risperidone, the half-life for the "active moiety" (risperidone +9-hydroxyrisperidone) was found to be about 20 hours in poor metabolizers. Risperidone exhibits linear elimination kinetics. Steady state is reached within 1 day for risperidone and within 5 days for the active fraction.

There has been considerable debate about the direct medication costs and the cost efficacy of novel antipsychotics such as risperidone. There are health economic studies that indicate reduced indirect costs associated with poor compliance, such as repeated acute ward admissions, but also perhaps a shift in resources towards community care (day hospital places and the like). Viale et al (1997) investigated costs associated with risperidone and found days in acute care inpatient facilities were reduced by 26 percent, and days in residential treatment were reduced by 57 percent. These reductions were accompanied by an increase in the use of lower-cost services, such as community and day hospital treatment.

Risperidone and other atypical antipsychotics appear to promote a higher quality of life compared to conventional antipsychotics. Physical well being, social life and everyday life have also been rated higher in a comparative study using risperidone (Franz et al, 1997). In one evaluation, compared to haloperidol, a conventional antipsychotic, risperidone-treated patients obtained more than twice as many quality-adjusted years as haloperidol patients and in addition risperidone was found to be cost-effective, (Chouinard & Albright, 1997). A U.S. evaluation of costs, including indirect ones came up with figures for treatment with haloperidol and risperidone (Keks, 1997). A robust decision-analytic model of schizophrenia suggested that the overall 1997 cost of treating a patient with risperidone would be $11,772.00 per year compared with $13,622.00 per year for haloperidol and that the cost per response is even more favourable for risperidone; $14,599.00 versus $23,040.00.Guidelines issued by the Australian Pharmaceutical Benefits Advisory Committee have been used to construct a model for comparing the cost-effectiveness of risperidone and haloperidol over a 2-year period in patients with chronic schizophrenia (Davies et al, 1998). Cost-effectiveness was determined by using decision-analytic modelling. The analyses included all significant direct costs (i.e., hospital costs; outpatient costs; and the cost of drugs, the services of health care professionals, and government-subsidised hostel accommodation). The cost for a given outcome was the sum of costs for all scenarios leading to that outcome. Cost-effectiveness was expressed as the total cost per favourable outcome, i.e. where the patient was responding to treatment at the end of the 2-year period. The probability of a patient experiencing a favourable outcome at the end of 2 years was 78.9% for risperidone versus 58.9% for

haloperidol. The total cost of treatment for 2 years was $15,549.00 for risperidone versus $18,332.00 for haloperidol. The expected cost per favourable outcome was $19,709.00 for risperidone and $31,104.00 for haloperidol. Risperidone was more cost-effective than haloperidol and therefore was "dominant" in pharmacoeconomic terms because it produced a higher proportion of favourable outcomes at lower cost.

Common side effects include insomnia (about 8% of patients), weight gain, agitation, anxiety and headache. Less frequent side effects include somnolence, tiredness, dizziness, poor concentration, nausea, and dysfunctions of erection, ejaculation and orgasm.

Orthostatic hypotension can occur particularly initially. Prolactin rises can induce galactorrhoea and gynaecomastia along with disturbances of the menstrual cycle and amenorrhoea, (Kim, Kim & lee, 1999). Prolactin rises are also documented in males (Markianos Hatzimanolis & Lykouras, 1999)Risperidone appears to have less potential for causing EPS than conventional antipsychotics and as such may be more suitable as a maintenance antipsychotic than conventional dopamine-blockers (Umbricht & Kane, 1996, Kopala et al, 1997). In a study completed by over two hundred chronic schizophrenic patients by Simpson & Lindenmayer (1997) the severity of EPS in a risperidone treated group as measured by the Extrapyramidal Symptom Rating Scale (ESRS) score did not differ significantly differ from placebo group. There was a linear relationship between mean change scores and increasing risperidone dose on 4 of the 12 ESRS subscales. However, even at 16 mg/day of risperidone, mean change scores were lower than in a group treated with haloperidol group. A linear relationship between increasing risperidone dose and use of antiparkinsonian medications was also apparent.In a study of more than a hundred elderly patients, often with co-morbid medical conditions risperidone was found to be a safe and effective antipsychotic (Zarate et al, 1997). In this study there were adverse events in 32% of the patients. These adverse events included hypotension (29%), extrapyramidal effects (11%), symptomatic orthostasis (10%), cardiac arrest (1.6%) with fatality (0.8%), and delirium (1.6%).There are several reports of neuroleptic malignant syndrome with risperidone, (Singer et al, 1995, Bonwick et al, 1996, Gleason, & Conigliaro, 1997, Bajjoka et al, 1997). There is at least one recent report associating a year's exposure to risperidone with tardive dyskinesia, although this was in a patient who had previously been exposed to classical antipsychotics (Silberbauer, 1998). There have been reports of priapism associated with risperidone (Tekell, Smith & Silva, 1995). There is at least one case report of risperidone causing sudden cardiac death (Ravin & Levinson, 1997). Annual adverse event monitoring in the UK has shown that the relative risk with risperidone compared to other antipsychotics is decreased (Tooley & Zuiderwijk, 1997). Annual reporting rates for tardive dyskinesia were 0.0006% of patients and neuroleptic malignant syndrome 0.017%. EPS reports were made for 0.2% of patients. It is unlikely though that all adverse events are reported, and these probably represent an underestimate of the true incidence.A variant tardive abnormal movement, rabbit syndrome, has been described with risperidone, (Levin & Heresco Levy, 1999). Rabbit syndrome is a rare side effect of chronic neuroleptic administration characterized by rapid, fine, rhythmic movements of the mouth along a vertical axis.Overdoses of up to 360 mg have been reported. Problems include sedation, tachycardia, hypotension and EPS. QT prolongation may occur on ECG. One of the first overdoses with risperidone was noted in 1993. ECG abnormalities were recorded, but there was no fatality, (Brown et al, 1993). Nevertheless fatalities have been reported, (Springfield & Bodiford, 1996).There may be interactions with carbamazepine, which decreases the plasma levels of the antipsychotic fraction of risperidone. Similar drugs that induce hepatic enzymes may have the same effect. Phenothiazines, tricyclic antidepressants, fluoxetine, haloperidol and some beta blockers can increase plasma concentrations of risperidone.No teratogenic effect has been yet noted, but caution should be exercised before prescribing in pregnancy. Risperidone is excreted in milk in animal studies. Women receiving risperidone should not therefore breast feed.

Extrapyramidal side effects, hyperprolactinemia, and sexual dysfunction are significantly more frequent with risperidone than olanzapine (Tran et al, 1997).

Patients who are treatment resistant as conventionally defined may probably be better treated with clozapine. However there is at least one recent study that suggests that a trial of risperidone may be worthwhile in conventional antipsychotic treatment resistance (Bondolfi et al, 1998). There appears to be little benefit to switching patients non-responsive to clozapine to risperidone, (Still et al, 1996). Clozapine is more effective than risperidone at reducing positive symptoms in resistant patients and is less likely to disturb the prolactin system (Breier et al, 1999).Compared to other antipsychotics it has moderate tendencies to cause weight gain. It is less likely to cause weight gain than olanzapine or clozapine (Wirshing et al, 1999)

Risperidone is one of a new generation of antipsychotic drugs with relatively fewer side effects and equal efficacy for florid 'positive' symptoms. The additional serotonergic actions of these new antipsychotics deliver further efficacy against 'negative' and affective symptoms of schizophrenia. There are however differences in the side effect profiles of the new antipsychotics and in some instances risperidone performs less well than others especially where higher doses are involved, inducing EPS. Despite their higher direct costs such antipsychotics, including particularly risperidone, have interesting economic arguments in their favour compared to earlier antipsychotics.

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Risperidone

http://bipolar-disorder.emedtv.com/risperidone/risperidone.html December 09, 2014

Risperidone is a medication used to treat bipolar disorder, schizophrenia, and irritability due to autism. This eMedTV resource offers an overview of risperidone ...

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NAMI: National Alliance on Mental Illness

http://www.nami.org/Template.cfm?Section=About_Medications&Template=/ContentManagement/ContentDisplay.cfm&ContentID=66283 December 09, 2014

Risperdal ® (risperidone) Brand name: Risperdal ® Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg. Orally disintegrating tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 ...

Generic name: risperidone (ris PER i done) All FDA black box warnings are at the end of this fact sheet. Please review before taking this medication. What is Risperdal® and what does it treat? Risperdione is a medication that works in the brain to treat schizophrenia. It is also known as a second generation antipsychotic (SGA) or atypical antipsychotic. Risperidone rebalances dopamine and serotonin to improve thinking, mood, and behavior. Hallucinations - imagined voices or images that seem real Delusions - beliefs that are not true (e.g., other people are reading your thoughts) Disorganized thinking or trouble organizing your thoughts and making sense Little desire to be around other people Risperidone may help some or all of these symptoms. Risperidone is also FDA approved for the following indications: Acute treatment of manic or mixed episodes of bipolar disorder This medication sheet will focus primarily on schizophrenia. You can find more information about bipolar disorder and autism spectrum disorders at . What is the most important information I should know about Risperdal®? Schizophrenia requires long-term treatment. Do not stop taking risperidone, even when you feel better. Only your healthcare provider can determine the length of risperidone treatment that is right for you. Missing doses of risperidone may increase your risk for a relapse in your symptoms. Do not stop taking risperidone or change your dose without talking to with your healthcare provider first. For risperidone to work properly, the tablet form should be taken everyday as ordered by your healthcare provider. Are there specific concerns about Risperdal® and pregnancy? If you are planning on becoming pregnant, notify your healthcare provider to best manage your medications. People living with schizophrenia who wish to become pregnant face important decisions. This is a complex decision since untreated schizophrenia has risks to the fetus, as well as the mother. It is important to discuss the risks and benefits of treatment with your doctor and caregivers. Caution is advised with breastfeeding since

risperidone does pass into breast milk. What should I discuss with my healthcare provider before taking Risperdal®? Symptoms of your condition that bother you the most If you have thoughts of suicide or harming yourself Medications you have taken in the past for your condition, whether they were effective or caused any adverse effects If you ever had muscle stiffness, shaking, tardive dyskinesia, neuroleptic malignant syndrome, or weight gain caused by a medication If you experience side effects from your medications, discuss them with your provider. Some side effects may pass with time, but others may require changes in the medication. Any psychiatric or medical problems you have, such as heart rhythm problems, long QT syndrome, heart attacks, diabetes, high cholesterol, or seizures If you have a family history of diabetes or heart disease All other medications you are currently taking (including over the counter products, herbal and nutritional supplements) and any medication allergies you have Other non-medication treatment you are receiving, such as talk therapy or substance abuse treatment. Your provider can explain how these different treatments work with the medication. If you are pregnant, plan to become pregnant, or are breast-feeding If you smoke, drink alcohol, or use illegal drugs How should I take Risperdal®? Risperidone tablets and solution are usually taken 1 or 2 times per day with or without food. Typically patients begin at a low dose of medicine and the dose is increased slowly over several weeks. The oral dose usually ranges from 1 mg to 6 mg. The dose of the injection usually ranges from 12.5 mg to 50 mg. Only your healthcare provider can determine the correct dose for you. Risperidone orally disintegrating tablets must remain in their original packaging. Open the package with clean dry hands before each dose. Do not try to put tablets in a pillbox if you take the orally disintegrating tablets. Risperidone orally disintegrating tablets will dissolve in your mouth within seconds and can be swallowed with or without liquid. Risperidone liquid should be measured with a dosing spoon or oral syringe, which you can get from your pharmacy. Use a calendar, pillbox, alarm clock, or cell phone alert to help you remember to take your medication. You may also ask a family member a friend to remind you or check in with you to be sure you are taking your medication. The long-acting injection form of risperidone is administered every 2 weeks. Your healthcare provider will administer these injections. What happens if I miss a dose of Risperdal®? If you miss a dose of risperidone, take it as soon as you remember, unless it is closer to the time of your next dose. Discuss this with your healthcare provider. Do not double your next dose or take more than what is prescribed. What should I avoid while taking Risperdal®? Avoid drinking alcohol or using illegal drugs while you are taking risperidone. They may decrease the benefits (e.g. worsen your confusion) and increase adverse effects (e.g. sedation) of the medication. What happens if I overdose with Risperdal®? If an overdose occurs call your doctor or 911. You may need urgent medical care. You may also contact the poison control center at 1-800-222-1222. A specific treatment to reverse the effects of risperidone does not exist. What are possible side effects of Risperdal®? Low blood pressure, feeling dizzy and increased heart rate, especially when standing up Fatigue, sleepiness, headache, constipation, and appetite increases are also common and more likely in children than in adults. Risperidone may increase the blood levels of a hormone called prolactin. Side effects of increased prolactin levels include females losing their period, production of breast milk and males losing their sex drive or possibly experiencing erectile problems. Long term (months or years) of elevated prolactin can lead to osteoporosis, or increased risk of bone fractures. Some people may develop muscle related side effects while taking risperidone. The technical terms for these are “extrapyramidal effects” (EPS) and “tardive dyskinesia” (TD). Symptoms of EPS include restlessness, tremor, and stiffness. TD symptoms include slow or jerky movements that one cannot control, often starting in the mouth with tongue rolling or chewing movements. Second generation antipsychotics (SGAs) increase the risk of weight gain, high blood sugar, and high cholesterol. This is also known as metabolic syndrome. Your healthcare provider may ask you for a blood sample to check your cholesterol, blood sugar, and hemoglobin A1c (a measure of blood sugar over time) while you take this medication. For more information including ideas for healthy eating and exercise, see the NAMI Hearts and Minds Program . For the relative risk of each medication and monitoring recommendations, see Table 2 in the Consensus Conference on Antipsychotic Drugs . SGAs have been linked with higher risk of death, strokes, and transient ischemic attacks (TIAs) in elderly people with behavior problems due to dementia. All antipsychotics have been associated with the risk of sudden cardiac death due to an arrhythmia (irregular heart beat). To minimize this risk, antipsychotic medications should be used in the smallest effective dose when the benefits outweigh the risks. Your doctor may order an EKG to monitor for irregular heart beat. Neuroleptic malignant syndrome is a rare, life threatening adverse effect of antipsychotics which occurs in <1% of patients. Symptoms include confusion, fever, extreme muscle stiffness, and sweating. If any of these symptoms occur, contact your healthcare provider immediately. Are there any risks of taking Risperdal® for long periods of time? Tardive dyskinesia (TD) is a side effect that develops with prolonged use of antipsychotics. Medications such as risperidone have been shown to have a lower risk of TD compared to older antipsychotics, such as Haldol® (haloperidol). If you develop symptoms of TD, such as grimacing, sucking, and smacking of lips, or other movements that you cannot control, contact your healthcare provider immediately. All patients taking either first or

second generation antipsychotics should have an Abnormal Involuntary Movement Scale (AIMS) completed regularly by their healthcare provider to monitor for TD. Second generation antipsychotics (SGAs) increase the risk of diabetes, weight gain, high cholesterol, and high triglycerides. (See “Serious Side Effects” section for monitoring recommendations.) What other medications may interact with Risperdal®? Risperidone may block the effects of agents used to treat Parkinson’s disease such as levodopa/carbidopa (Sinemet®), bromocriptine, pramipexole (Mirapex®), ropinirole (Requip®), and others. Risperidone may lower your blood pressure. Medications used to lower blood pressure may increase this effect and increase your risk of falling. Propranolol (Inderal®) is an example of this type of medication. The following medications may increase the levels and effects of risperidone: divalproex sodium (Depakote®), fluoxetine (Prozac®), paroxetine (Paxil®), and verapamil (Calan®). The following medications may decrease the levels and effects of risperidone: carbamazepine (Tegretol®, Equatro®), phenytoin (Dilantin®), phenobarbital, or rifampin (Rifadin®). How long does it take for Risperdal® to work? It is very important to tell your doctor how you feel things are going during the first few weeks after you start taking risperidone. It will probably take several weeks to see big enough changes in your symptoms to decide if risperidone is the right medication for you. Antipsychotic treatment is generally needed lifelong for persons with schizophrenia. Your doctor can best discuss the duration of treatment you need based on your symptoms and illness. Hallucinations, disorganized thinking, and delusions may improve in the first 1-2 weeks Sometimes these symptoms do not completely go away Motivation and desire to be around other people can take at least 1-2 weeks to improve Symptoms continue to get better the longer you take risperidone It may take 2-3 months before you get the full benefit of risperidone Both first generation (typical) and second generation (atypical) antipsychotics are associated with an increased risk of mortality in elderly patients when used for dementia related psychosis. Although there were multiple causes of death in studies, most deaths appeared to be due to cardiovascular causes (e.g. sudden cardiac death) or infection (e.g. pneumonia). Antipsychotics are not indicated for the treatment of dementia-related psychosis.

Risperdal (risperidone)

http://www.netdoctor.co.uk/brain-and-nervous-system/medicines/risperdal.html December 09, 2014

Risperdal tablets, liquid and quicklets all contain the active ingredient risperidone, which is a type of medicine known as an atypical antipsychotic.

Risperdal tablets, liquid and quicklets all contain the active ingredient risperidone, which is a type of medicine known as an atypical antipsychotic. Risperidone is also available without a brand name, ie as the generic medicine.

Risperidone works in the brain, where it affects various neurotransmitters, in particular dopamine and serotonin (5HT). Neurotransmitters are chemicals that are stored in nerve cells and are involved in transmitting messages between the nerve cells.

Dopamine and serotonin are neurotransmitters known to be involved in regulating mood and behaviour, amongst other things. Psychotic illness is considered to be caused by disturbances in the activity of neurotransmitters (mainly dopamine) in the brain. Schizophrenia is known to be associated with an overactivity of dopamine in the brain, and this may be associated with the delusions and hallucinations that are a feature of this disease.

Risperidone works by blocking the receptors in the brain that dopamine acts on. This prevents the excessive activity of dopamine and helps to control schizophrenia.

Schizophrenic patients may experience 'positive symptoms' (such as hallucinations, disturbances of thought, hostility) and/or 'negative symptoms' (such as lack of emotion and social withdrawal). Risperidone is effective in relieving both positive and negative symptoms of schizophrenia, whereas the conventional antipsychotics are usually less effective against the negative symptoms.

Risperidone also relieves 'affective symptoms' that are associated with schizophrenia, such as depression, guilt feelings or anxiety.

Risperidone is used by specialists to treat episodes of mania in people with the psychiatric illness, bipolar affective disorder (manic depression).

Risperidone may also be used by specialists to treat severe aggressive behaviour in elderly people with Alzheimer's disease, and in intellectually disabled children with conduct disorder.

Risperidone can be taken as liquid, conventional tablets or Risperdal quicklets. Risperdal quicklets are tablets that are designed to dissolve on the tongue and be swallowed with the saliva, without the need for water.

For the treatment of schizophrenia, risperidone can also be given as a depot injection that lasts for two weeks. See the link to Risperdal consta at the end of this factsheet for more information.

This medicine should not be used if you are allergic to one or any of its ingredients. Please inform your doctor or pharmacist if you have previously experienced such an allergy.

If you feel you have experienced an allergic reaction, stop using this medicine and inform your doctor or pharmacist immediately.

Certain medicines should not be used during pregnancy or breastfeeding. However, other medicines may be safely used in pregnancy or breastfeeding providing the benefits to the mother outweigh the risks to the unborn baby. Always inform your doctor if you are pregnant or planning a pregnancy, before using any medicine.

Medicines and their possible side effects can affect individual people in different ways. The following are some of the side effects that are known to be associated with this medicine. Just because a side effect is stated here does not mean that all people using this medicine will experience that or any side effect.

The side effects listed above do not include all of the side effects reported by the medicine's manufacturer.

For more information about any other possible risks associated with this medicine, please read the information provided with the medicine or consult your doctor or pharmacist.

It is important to tell your doctor or pharmacist what medicines you are already taking, including those bought without a prescription and herbal medicines, before you start treatment with this medicine. Similarly, check with your doctor or pharmacist before taking any new medicines while taking this one, to make sure that the combination is safe.

There may be an increased risk of drowsiness and sedation if risperidone is taken with any of the following (which can also cause drowsiness):

Risperidone may enhance the blood pressure-lowering effects of medicines that lower blood pressure, including medicines used to treat high blood pressure (antihypertensives) and medicines that lower blood pressure as a side effect, eg benzodiazepines. If you are taking medicines that lower blood pressure you should tell your doctor if you feel dizzy or faint after starting treatment with this medicine, as your doses may need adjusting.

There may be an increased risk of abnormal heart rhythms (prolonged QT interval on a heart monitoring trace or ECG) if this medicine is taken in combination with any of the following medicines:

There may also be an increased risk of a prolonged QT interval if medicines that can alter the levels of salts such as potassium or magnesium in the blood, eg diuretics such as furosemide, are taken in combination with risperidone.

Risperidone may oppose the effect of medicines for Parkinson's disease that work by stimulating dopamine receptors in the brain, for example levodopa, ropinirole, pergolide, bromocriptine.

Risperidone may oppose the effect of anticonvulsant medicines used to treat epilepsy.

Risperidone may increase blood sugar levels and disturb the control of diabetes. People with diabetes may need an adjustment in the dose of their antidiabetic medication.

Risperidone may oppose the effect of histamine (used to treat leukaemia) and is not recommended for people having this treatment.

The following medicines may speed up the breakdown of risperidone in the body and so could make it less effective. If you take any of these medicines your doctor may need to increase your dose of risperidone:

The following medicines may slow down the breakdown of risperidone in the body and so could increase the amount in the blood. If you take any of these medicines your doctor may need to prescribe a lower dose of risperidone:

This medicine should not be used in combination with paliperidone.

Risperidone tablets are also available without a brand name, ie as the generic medicine.

Risperdal (Risperidone)

http://huddersfield1.co.uk/depression/risperidone.htm December 09, 2014

Huddersfield One Depression - Risperidone Tablets are used to treat conditions which affect the way you think, feel and/or act. These conditions may cause symptoms ...

This product is available using any of the above names but will be referred to as Risperidone 1mg / 2mg Tablets throughout the following: Patient Information Leaflet

Please read this information about Risperidone 1mg / 2mg Tablets carefully before you start taking your tablets.

It contains all the information you should need to know. If you have any further questions or are not sure about anything, ask your doctor or pharmacist.

Please keep this information in a safe place, you may wish to refer to it again. The medicine is called Risperidone Tablets. Each film-coated tablet contains 1 mg of the active ingredient risperidone, and is oblong and white. It is coded 'RIS 1' with a breakline on one side and plain on the reverse.

OR

The medicine is called Risperidone 2mg Each film-coated tablet contains 2 mg of the active ingredient risperidone, and is oblong and white. It is coded 'RIS 2' with a breakline on one side and plain on the reverse. Risperidone 1mg Tablets also contain the following:

lactose, maize starch, microcrystalline cellulose, hypromellose, magnesium stearate, colloidal anhydrous silica, sodium lauryl sulphate and propylene glycol. Risperidone 2mg Tablets also contain the following:

lactose, maize starch, microcrystalline cellulose, hypromellose, magnesium stearate, colloidal anhydrous silica, sodium lauryl sulphate, propylene glycol, titanium dioxide (E171), talc and sunset yellow FCF aluminium lake (E110). Risperidone l mg / 2mg Tablets are available in blister packs containing 60 tablets. Risperidone belongs to a group of medicines called antipsychotics and is used to improve thoughts, feeling andlor behaviour when these are disturbed In certain medical conditions. Why you need to take this medicine:

Risperidone Tablets are used to treat conditions which affect the way you think, feel and/or act. These conditions may cause symptoms such as confusion, hallucinations (eg hearing, sensing or seeing things, which are not there), delusions, paranoia (unusual suspiciousness), and emotional and social withdrawal. People with these conditions may also feel depressed, guilty or anxious or tense. Risperidone Tablets may be taken for acute (sudden) and chronic (long-lasting) disorders. Before you take your medicine:

Make sure it is safe for you to take Risperidone Tablets If you answer YES to any of the following questions DO NOT use Risperidone l mg / 2mg Tablets. Tell your doctor. Have you ever had an allergic reaction to Risperidone Tablets, risperidone or any of the other ingredients of these tablets? (an allergic reaction may include rash, itching, swollen lips or face, shortness of breath). Check to see if any of the following apply to you, and consult your doctor before starting to take the medicine if the answer is YES to any of them: Are you pregnant, think you might be pregnant or are you trying to become pregnant? If so you should talk to your doctor who will decide if you should take Risperidone 1mg / 2mg Tablets. It you suffer from any of the following problems, you may need to be more closely supervised during treatment and the dosage may need to be altered. Do you suffer from heart or blood vessel disease? Do you suffer from kidney or liver disease? Do you suffer from Parkinson's disease or epilepsy? Are you taking carbamazepine (used to treat epilepsy or facial neuralgia - severe pain attacks in the face)? This may change the effect of Risperidone l mg / 2mg Tablets. Tell your doctor if you start or stop taking this drug as you may need a different dose of Risiperidione 1mg 1 2mg Tablets. Are you taking any medicines for anxiety, medicines to help you sleep (tranquillisers), certain painkillers, antidepressants or

some antihistamines (e.g. chiorpheniramine)? Taking Risperidone 1mg / 2rng Tablets as well may make you feel drowsy. Only take any of these as well as Risperidone Tablets if your doctor tells you that you can. Are you taking any medicines for Parkinson's disease? You should tell your doctor if you are taking any other medicines whether prescribed for or bought without prescription. If you are not sure what to do, check with your doctor or pharmacist. Warnings:

Risperidone 1mg / 2mg Tablets may make you put on weight, so you should try to eat moderately while taking these tablets. You should be careful how much alcohol you drink whilst taking Risperidone Tablets. The combined effect of alcohol and the tablets may make you feel drowsy. As with other drugs of this type, Risperidone Tablets could cause uncontrollable movements, mainly of the face or tongue. If this happens, consult your doctor. Very rarely Risperidone Tablets might also cause fever, faster breathing, sweating, muscle stiffness and reduced consciousness. If any of these occur, STOP taking the tablets and contact your doctor immediately. Risperidone Tablets may affect your alertness so you should not drive or operate machinery until the doctor sees how the tablets affect you. Allergy is more common in those people who are allergic to aspirin. When to take your tablets:

Follow the doctor's instructions, and check the directions on the pharmacy label, which should tell you how many tablets to take in a day. If it does not or you are unsure, ask your doctor or pharmacist. It does not matter whether you take Risperidone Tablets with or without food. Swallow the correct number of tablets with some liquid. This will vary from person to person and your doctor will adjust the number and strength of the tablets to suit you. Do not be surprised therefore if you are given differently-coloured tablets from time to time. It is very important that you take the correct amount. The dose for adults and the elderly should be individually set by your doctor and if necessary increased only gradually. Always read the label on your medicine and follow your doctor's instructions carefully. Ask your pharmacist or nurse if you are not sure about anything. Risperidone Tablets is only for those aged 15 years and over.

The dose of Risperidone Tablets will be started gradually over the first days of treatment. Your doctor will probably recommend the following dosage to start with: Day 1: 2mg (as a single dose or as 1 mg in the morning and 1 mg in the evening); Day 2: 4mg (as a single dose or as 2mg in the morning and 2mg in the evening). However, if you have not used Risperidone Tablets before, your doctor may recommend a more gradual increase. The dosage will then be set to suit your needs but will normally be 4mg to 6mg a day, either as a single dose or split into two doses, one to be taken in the morning and one to be taken in the evening. Some patients may require less than 4mg for a good effect. Important:

Never take more than a total of 16mg per day. If you are elderly or have a liver or kidney disorder you should take half the above doses. You will be told how many tablets you need to take. Do not stop your treatment just because you feet better. It is important that you carry on taking Risperidone Tablets for as long as your doctor tells you to. What to do if an overdose is taken:

If too many tablets are taken consult your doctor or get someone to take you to your nearest hospital casualty department IMMEDIATELY. Do not drive yourself. Remember to take the leaflet and any tablets with you, so that the doctor in charge knows what you have taken. What to do if you miss a dose:

If you miss a dose in the initial treatment period, take it as soon as possible instead of your next dose and then take the remaining doses in the order described above. Then continue at whatever dose your doctor has prescribed for you. If you miss a tablet after the first few days, do not take the missed dose but take your next dose as usual and continue your course. If you are not sure what to do, ask your doctor or Pharmacist Side-Effects:

As with all medicines Risperidone Tablets can cause unwanted side-effects in some patients. The tablets are generally well-tolerated. There are usually few side-effects when Risperidone Tablets are taken in the way your doctor, nurse or pharmacist has prescribed. Sometimes Risperidone Tablets may cause side effects such as:

sleeplessness, agitation, anxiety and headache. Occasionally the following effects may occur:

sleepiness, tiredness, concentration difficulties, blurred vision, dizziness, indigestion, nausea (feeling sick), vomiting (being sick), stomach ache, constipation, sexual potency problems, leakage of urine, runny or blocked nose, liver problems, local skin rash or swelling, or other allergic reactions suck as itching, swollen face or lips, shortness of breath. Swelling of the ankles may occur. Some people may feel dizzy in the early stages of treatment, especially when getting up from a lying or sitting position. This will usually pass off on its own but if it does not, tell your doctor. Sometimes trembling, pronounced

muscle stiffness or spasm, slowness of movement, excess saliva or restlessness can occur but this will usually disappear if your dose of Risperidone Tablets is reduced by your doctor or if your doctor prescribes an additional medicine. After prolonged use, women may suffer from milk secretion, an absence of their monthly period or changes in the regularity of their periods. Men may experience breast swelling. If these persist, tell your doctor. Risperidone Tablets may make you put on weight so you should try to eat moderately while taking this medicine. Occasionally mild blood cell changes have been reported. In some cases,

the blood pressure may fall slightly in the early stages of treatment, resulting in dizziness. This will usually pass off automatically. Somewhat later in treatment increased blood pressure may occur, but this is very rare. In rare cases,

Risperidone Tablets may cause a desire to drink large amounts of water. You might also experience marked changes in your body temperature. Rare cases of convulsions have also occurred. If any of these occurs contact your doctor as soon as possible. Very rarely,

Risperidone Tablets might cause fever, faster breathing, sweating, muscle stiffness and reduced consciousness. If this occurs, stop taking the tablets and contact a doctor at once. As with other drugs of this type, Risperidone Tablets could cause uncontrollable movements, mainly of the face or tongue. Should this occur, talk to your doctor. You should also see your doctor if you feel any other unusual or unexpected side effects not mentioned above during or after taking Risperidone Tablets. He or she (or it?) will have more information about Risperidone Tablets and will tell you what to do. Expiry Date:

Do not use after the expiry date printed on the carton label or blister strip. Storage:

Risperidone Tablets should be stored below30*C in a dry place and protected from light. The tablets should be kept in the original container. KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN.

If your doctor tells you to stop taking the tablets, please take them back to the pharmacist for safe disposal. Only keep the tablets if your doctor tells you to. If the tablets become discoloured or show signs of any deterioration, you should seek the advice of your pharmacist who will advise you what to do. IMPORTANT.

This medicine is for YOUR use only. It can only be prescribed by a doctor. Never give it to anyone else. It may harm them even if their symptoms are the same as yours. This is not the complete information about Risperidone. If you have any questions, or are not sure about anything, ask your doctor or pharmacist who has access to additional information.

Risperidone

http://www.webmd.boots.com/children/autism-risperidone December 09, 2014

Risperidone is a newer type of antipsychotic drug. It may have fewer side effects than older drugs of this kind. One brand name is Risperdal.

This information is for people who have a child with autism. It tells you about risperidone, a treatment used for autism. It is based on the best and most up-to-date research.

Yes. Children with autism who take risperidone are likely to be less irritable. This drug works as a short-term treatment for children who have tantrums, fight, or hurt themselves.

But can cause side effects. These include putting on weight, having shaking you can't control (called tremors), and feeling sleepy.

In the UK, only specialists such as child psychiatrists and paediatricians prescribe risperidone for children with autism.

Risperidone is an antipsychotic drug. It's usually used to treat mental health problems such as schizophrenia. But some specialists may prescribe it for children with autism if they think it might help.

Risperidone is a newer type of antipsychotic drug. It may have fewer side effects than older drugs of this kind.

One brand name is . It comes as tablets, a liquid, or injections.

Taking risperidone reduces symptoms of autism in about 7 in 10 children who have tantrums, fight, or hurt themselves. [91] The drug can also help if your child is very irritable or hyperactive.

One summary of the evidence said risperidone helped children with autism to: [92]

Risperidone works by calming down activity in your brain. It does this by blocking certain chemicals called neurotransmitters. These chemicals help signals travel between nerve cells. Risperidone blocks the ones called serotonin and dopamine.

Your child may have symptoms such as having tantrums, fighting, and trying to hurt themselves, because there is too much serotonin or dopamine in their brain. So blocking these chemicals might help.

Yes. Risperidone may make your child put on weight. In one study, children taking the drug gained on average 2.7 kilograms (about 6 pounds) over eight weeks. [91] Children who took a dummy treatment (a placebo) for comparison gained only 0.8 kilograms (about 2 pounds).

Children taking risperidone can also have tremors. [91] That means they have shaking they can't control. And the drug can make your child sleepy too. One study found that more than 7 in 10 children taking risperidone got sleepy. [91] Your doctor may suggest your child take this medicine in the afternoon rather than in the morning. That way, your child's school day won't be so affected if they get drowsy. [93]

Risperidone can also make your child's blood pressure go up a bit and make their heart beat faster. [93] About 1 in 10 children who take risperidone get a fast heartbeat.

RxMed: Pharmaceutical Information

http://www.rxmed.com/b.main/b2.pharmaceutical/b2.1.monographs/CPS-%20Monographs/CPS-%20(General%20Monographs-%20R)/RISPERDAL.html December 09, 2014

RISPERDAL® Oral Solution RISPERDAL® Tablets : Janssen-Ortho : Risperidone Tartrate: Risperidone : Antipsychotic Agent Action And Clinical Pharmacology: Risperidone ...

Risperidone, a benzisoxazole derivative, is a novel antipsychotic drug which binds with high affinity to the serotonin type 2 (5-HT2), dopamine D2, and a1-adrenergic receptors. Risperidone binds with a lower affinity to the a2-adrenergic and histamine H1 receptors. Risperidone does not bind to dopamine D1 or muscarinic cholinergic receptors.

Receptor occupancy was also demonstrated in vivo in humans. Using positron emission tomography, risperidone was shown to block both 5-HT2 and dopamine D2 receptors in 3 healthy volunteers.

Pharmacokinetics: Risperidone was well absorbed after oral administration, had high bioavailability, and showed dose-proportionality in the therapeutic dose range, although inter-individual plasma concentrations varied considerably. Food did not affect the extent of absorption, thus, risperidone can be given with or without meals.

The bioequivalence of the oral formulations (oral solution and tablets) has been demonstrated. A summary table of comparative bioavailability data for unchanged risperidone is presented in Table I.

Peak plasma concentrations of parent drug are reached within 1 to 2 hours after drug intake. Risperidone is mainly metabolized via hydroxylation and oxidative N-dealkylation. The major metabolite is 9-hydroxy-risperidone which has similar activity to the parent drug. Consequently, the clinical effect is brought about by the active moiety, namely risperidone plus 9-hydroxy-risperidone.

The hydroxylation of risperidone is dependent upon debrisoquine 4-hydroxylase i.e., the metabolism of risperidone is sensitive to the debrisoquine hydroxylation type genetic polymorphism. Consequently, the concentrations of parent drug and active metabolite differ substantially in extensive and poor metabolizers. However, the concentration of the active moiety (risperidone plus 9-hydroxy-risperidone) did not differ substantially between extensive and poor metabolizers, and elimination half-lives were similar in all subjects (approximately 20 to 24 hours).

Risperidone is rapidly distributed. The volume of distribution is 1 to 2 L/kg. Steady-state concentrations of risperidone and the active moiety were reached within 1 to 2 days and 5 to 6 days, respectively. In plasma, risperidone is bound to albumin and alpha1-acid glycoprotein (AGP). The plasma protein

binding of risperidone is approximately 88%, that of the metabolite 77%. One week after administration, 70% of the dose is excreted in the urine and 14% in the feces. In urine, risperidone plus 9-hydroxy-risperidone represent 35 to 45% of the dose. The remainder is inactive metabolites.

The results indicate that a 1 mg dose of risperidone produced modest pharmacokinetic changes in elderly subjects. In patients with impaired renal function, the changes were substantial; Cmax and AUC were increased, half-life prolonged and clearance decreased.

In patients with impaired liver function, the unbound fraction of risperidone was somewhat increased due to diminished concentration of both a1-AGP and albumin.

Clinical Studies: In controlled trials, risperidone was evaluated in a dose range of 1 to 16 mg/day and compared to both placebo and haloperidol. The studies indicated that risperidone is an effective antipsychotic agent improving both positive and negative symptoms. Optimal therapeutic response was seen in the 4 to 8 mg/day dose range, indicating a bell-shaped dose-response relationship. Parkinsonian side effects were mild but dose-related. Risperidone elevated serum prolactin levels. Due to the a1-adrenergic blocking activity, orthostatic hypotension with compensatory tachycardia was also observed.

For the management of manifestations of schizophrenia and related psychotic disorders. In controlled clinical trials, risperidone was found to improve both positive and negative symptoms of schizophrenia.

In patients with a known hypersensitivity to the drug or the excipients of the product.
tag_WarningWarnings

Cardiovascular: During clinical trials, risperidone has been observed to cause orthostatic hypotension and tachycardia, especially during the initial dose titration period and the first few weeks of treatment. Rare cases of syncope, cardiac arrhythmias and first degree AV-block have been reported. The likelihood of excessive hypotension or syncope can be minimized by limiting the initial dose of the drug to 1 mg b.i.d. in adult patients and to 0.5 mg b.i.d. in special patient populations, and by increasing the dose slowly (see Dosage). A dose reduction should be considered if hypotension occurs.

Patients with a history of clinically significant cardiac disorders were excluded from clinical trials. Therefore, risperidone should be used with caution in patients with cardiovascular diseases (e.g., heart failure, myocardial infarction, cerebrovascular disease, conduction abnormalities) and other conditions such as dehydration and hypovolemia. Special care should be taken to avoid hypotension in patients with a history of cerebrovascular insufficiency or ischemic heart disease, and in patients taking medications to lower blood pressure.

Neuroleptic Malignant Syndrome (NMS): Neuroleptic malignant syndrome is a potentially fatal symptom complex that has been reported in association with neuroleptic drugs, including risperidone.

Clinical manifestations of NMS are hyperthermia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular blood pressure, tachycardia, cardiac arrhythmias and diaphoresis). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure.

In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms. Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary CNS pathology.

The management of NMS should include: 1) immediate discontinuation of all antipsychotic drugs including risperidone, and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrence of NMS has been reported.

Tardive Dyskinesia (TD): A syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with conventional antipsychotic drugs. Although TD appears

to be most prevalent in the elderly, especially elderly females, it is impossible to predict at the onset of treatment which patients are likely to develop TD.

It has been suggested that the occurrence of parkinsonian side effects is a predictor for the development of TD. In clinical studies, the observed incidence of drug-induced parkinsonism was lower with risperidone than with haloperidol. In the optimal clinical dose range, the difference between risperidone and haloperidol was significant. The risk of developing TD may be less with risperidone.

The risk of developing TD and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although less commonly, after relatively brief periods of treatment at low doses. There is no known treatment for established cases of TD. The syndrome may remit, partially or completely, if antipsychotic drug treatment is withdrawn. Antipsychotic drug treatment itself, however, may suppress the signs and symptoms of TD, thereby masking the underlying process. The effect of symptom suppression upon the long-term course of TD is unknown.

In view of these considerations, risperidone should be prescribed in a manner that is most likely to minimize the risk of TD. As with any antipsychotic drug, risperidone should be reserved for patients who appear to be obtaining substantial benefit from the drug. In such patients, the smallest dose and the shortest duration of treatment should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of TD develop during treatment with risperidone, withdrawal of the drug should be considered. However, some patients may require treatment with risperidone despite the presence of the syndrome.

Occupational Hazards: Interference with Mental Alertness: Risperidone may interfere with activities requiring mental alertness. Therefore, patients should be cautioned not to drive or operate machinery until their individual susceptibility is known.

Seizures: Conventional neuroleptics are known to lower seizure threshold. In clinical trials, seizures have occurred in a few risperidone-treated patients. Therefore, caution should be used in administering risperidone to patients having a history of seizures or other predisposing factors.

The risk for potential interaction between risperidone and other drugs has not been evaluated systematically. Risperidone may enhance the effects of alcohol, centrally-acting drugs, as well as the effects of antihypertensive agents. Because of its potential for inducing hypotension, risperidone may enhance the hypotensive effects of other therapeutic agents with this potential.

Risperidone may antagonize the effects of levodopa and dopamine agonists.

Carbamazepine has been shown to decrease substantially the plasma levels of risperidone and its active metabolite, 9-hydroxy-risperidone. Similar effects may be observed with other hepatic enzyme inducers. Consequently, in the presence of carbamazepine or other hepatic enzyme inducers, the dose of risperidone may have to be adjusted. On discontinuation of these drugs, the dosage of risperidone should be re-evaluated and, if necessary, decreased.

The metabolism of risperidone, a substrate of the hepatic cytochrome P450 isozyme (P450IID6), is affected by the debrisoquine hydroxylation polymorphism (see Pharmacology, Pharmacokinetics). Potential interaction between risperidone and drugs that are also substrates of this enzyme, namely phenothiazines, tricyclic antidepressants, selective serotonin reuptake inhibitors, and some beta-blockers, should be considered.

In vitro studies, in which risperidone was given in the presence of various, highly protein-bound agents, indicated that clinically relevant changes in protein binding would not occur either for risperidone or for any of the drugs tested.

Endocrine Effects: Antipsychotic drugs elevate prolactin levels with the effect persisting during chronic administration. In controlled clinical trials, risperidone elevated substantially serum prolactin levels; in female patients, mean levels ranged between 48 and 57 ng/mL at doses ranging from 4 to 16 mg/day. The prolactin levels were considerably higher in risperidone-treated patients than in haloperidol-treated patients. Since tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent in vitro, risperidone should only be administered to patients with previously

detected breast cancer if the benefits outweigh the potential risks. Caution should also be exercised when considering risperidone treatment in patients with pituitary tumors. Possible manifestations associated with elevated prolactin levels are amenorrhea, galactorrhea, and menorrhagia (see Adverse Effects).

In carcinogenicity studies, the administration of risperidone resulted in an increase in the incidence of mammary neoplasms in both rats and mice. In addition, adenomas of the endocrine pancreas in male rats and pituitary adenomas in female mice have been noted. These changes have been attributed to elevated prolactin levels and have also been observed with other dopamine receptor antagonists. To date, neither clinical studies nor epidemiological studies have shown an association between chronic administration of these drugs and mammary tumorigenesis.

With continued treatment, weight gain (mean: 2.3 kg in long-term studies) has been seen.

Pregnancy: The safety of risperidone for use during pregnancy has not been established. In animal studies, risperidone did not show direct reproductive toxicity. However, due to its prolactin elevating and CNS depressant activities, reproductive performance and pup survival were adversely affected in rats. Risperidone was not teratogenic in either rats or rabbits.

Risperidone should not be used during pregnancy unless the expected benefits outweigh the potential risks to the fetus.

Lactation: It is not known whether risperidone is excreted in human milk. Risperidone appeared in the milk of lactating dogs. The concentration of risperidone was similar in milk and plasma, while that of 9-hydroxy-risperidone was higher in the milk than in plasma.

Nursing should not be undertaken while a patient is receiving risperidone.

Geriatrics: Since the elimination of risperidone is somewhat slower in the elderly (see Pharmacology, Pharmacokinetics), doses exceeding 3 mg/day are not recommended in these patients (see Dosage).

Children: The safety and efficacy of risperidone in children under the age of 18 have not been established.

Patients with Hepatic Impairment: To date, clinical experience is lacking in this patient population. Although the pharmacokinetics in patients with liver insufficiency were comparable to those in young volunteers, the free fraction of risperidone was increased. Since this may lead to a more pronounced pharmacological effect, it is recommended to halve the starting dose and the subsequent dose increments (see Dosage).

Patients with Renal Impairment: The pharmacokinetics of risperidone were significantly altered in patients with renal disease (see Pharmacology, Pharmacokinetics). Since clinical experience is lacking in this patient population, dosage recommendations cannot be made at this time.

Patients with Parkinson's Disease: Risperidone, like other dopamine antagonists, may cause a deterioration in the condition of parkinsonian patients and should therefore be used with caution.

The most frequent adverse reactions observed during clinical trials with risperidone were insomnia, agitation, extrapyramidal disorder, anxiety, and headache (see Tables III and IV). In some instances it has been difficult to differentiate adverse events from symptoms of the underlying psychosis.

The most serious adverse reactions were rare cases of syncope, cardiac arrhythmias, first degree AV-block, and seizures.

An estimated 9% of approximately 1 800 patients who received risperidone in controlled clinical trials discontinued treatment due to adverse reactions. The more common events causing discontinuation included: Psychiatric (4.1%): primarily psychosis, agitation, suicide attempt, somnolence. Neurological (3.2%): primarily extrapyramidal disorder, dizziness. Cardiovascular (1.2%): primarily hypotension. Other events leading to discontinuation included: tachycardia/palpitations (0.6%), nervousness (0.4%), nausea (0.3%) and insomnia (0.3%).

Parkinsonian side effects were usually mild and were reversible upon dose reduction and/or administration of antiparkinsonian medication.

Occasionally, hypotension (including orthostatic), and tachycardia (including reflex tachycardia) have been observed following the administration of risperidone (see Warnings).

Risperidone elevated plasma prolactin levels. Associated manifestations, namely amenorrhea, galactorrhea, and menorrhagia, have occurred.

Weight gain, erectile dysfunction, ejaculatory dysfunction, orgastic dysfunction, and rash have also been observed during treatment with risperidone. In one study, in which testosterone levels were measured, testosterone decreased below the normal range in 6 out of 85 patients.

As with classical neuroleptics, cases of water intoxication, either due to polydipsia or to inappropriate secretion of antidiuretic hormone (ADH), have occasionally been reported during treatment with risperidone.

Adverse Events for North American Studies: Table III enumerates adverse events that occurred at an incidence of 1% or more, and were at least as frequent among risperidone-treated patients receiving doses of Ł10 mg/day than among placebo-treated patients in the pooled results of two 6- to 8-week controlled trials. Patients received risperidone doses of 2, 6, 10, or 16 mg/day in the dose comparison trial, or up to a maximum dose of 10 mg/day in the titration study. This table shows the percentage of patients in each dose group (Ł10 mg/day or 16 mg/day) who spontaneously reported at least one episode of an event at some time during their treatment. Patients given doses of 2, 6, or 10 mg did not differ substantially in these rates. Reported adverse events were classified using the World Health Organization preferred terms.

Adverse Reactions During Long-term Treatment: Long-term treatment with risperidone was carried out in 386 chronic schizophrenic patients, with 213 patients receiving the drug for at least 1 year. The UKU side effect rating scale was used to elicit adverse events.

Listed (in decreasing order) are those events which showed deterioration during treatment compared to baseline in at least 10% of patients. Psychic: asthenia/lassitude/increased fatiguability, concentration difficulties, sleepiness/sedation, reduced duration of sleep, increased duration of sleep, failing memory, increased dream activity. Autonomic: orthostatic dizziness, constipation, nausea/vomiting, polyuria/polydipsia, palpitations/tachycardia, reduced salivation, accommodation disturbances, increased tendency to sweating, diarrhea. Other: weight gain, weight loss, amenorrhea, ejaculatory dysfunction, erectile dysfunction, diminished sexual desire, tension headache, increased sexual desire, orgastic dysfunction.

Postmarketing: International postmarketing reporting revealed the following adverse drug reactions during risperidone treatment: edema, increased hepatic enzyme levels, skin manifestations of allergy including a case of Stevens-Johnson syndrome, systemic manifestations of allergy including a case of anaphylactic shock, neuroleptic malignant syndrome and rare cases of tardive dyskinesia, hypertension, leukopenia and priapism. Rarely, mild to moderate neutropenia associated in a few cases with thrombopenia has been reported. To date, a causal relationship to risperidone has not been established. As with other neuroleptics, sudden deaths have been reported during risperidone treatment. Most of the patients had pre-existing cardiovascular disease or were morbidly obese. A relationship to risperidone has not been established at this time.

Symptoms: Cases of overdosing have been reported with risperidone; the estimated doses were between 20 and 360 mg. Symptoms observed were due to excessive pharmacological effects, namely drowsiness and sedation, tachycardia and hypotension, and extrapyramidal symptoms. In 1 case (240 mg) hyponatremia and hypokalemia were observed, with prolonged QTc and widened QRS complex on the ECG. Additionally, hypokalemia and prolonged QT interval were observed in 1 patient who ingested 360 mg of risperidone. tag_Treatment

Treatment: Since there is no specific antidote to risperidone, treatment is primarily supportive. Gastric lavage (after intubation, if the patient is unconscious) and administration of activated charcoal together with a laxative should be considered.

A patent airway must be established and maintained to ensure adequate oxygenation and ventilation. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias. Hypotension and circulatory collapse may be counteracted by use of i.v. fluids. Epinephrine should not be used. In cases of severe extrapyramidal reactions, antiparkinsonian medication should be administered. Close medical

supervision and monitoring should continue until the patient recovers.

In managing overdosage, the physician should consider the possibility of multiple drug involvement.

In order to avoid orthostatic hypotension, the dose of risperidone should be titrated gradually.

Adults: Patients should be titrated gradually over 3 days on a b.i.d. schedule to a 6 mg daily dose, generally beginning with a 2 mg daily dose. The dosage should be increased to 4 mg on the second day and to 6 mg on the third day. Some patients may benefit from lower initial doses and/or a slower titration schedule.

Further dosage adjustments, if indicated, should generally occur at intervals of not less than 1 week since steady state for the active metabolite would not be achieved for approximately 1 week in the typical patient. When dosage adjustments are necessary, small dose increments/decrements are recommended.

Once a therapeutically effective maintenance dose has been established, risperidone may be administered once daily or twice daily.

In controlled clinical trials, optimal therapeutic effects were seen in the 4 to 8 mg/day dose range. Some patients may need higher doses, while in some patients further dosage increases may result in decreased therapeutic effect. Higher doses were associated with more extrapyramidal symptoms and other adverse effects. Since the safety of doses above 16 mg total daily dose has not been evaluated, doses above this level should not be used.

Geriatrics: In elderly patients, the doses of risperidone should be titrated slowly from a 0.5 mg b.i.d. starting dose to a maximum daily dose of 3 mg. Since the elimination of risperidone is somewhat slower in these patients, the potential for accumulation should be considered (see Pharmacology, Pharmacokinetics).

Postmarketing, treatment with risperidone in the elderly has been reported in publications for over 300 patients.

Patients Prone to Hypotension: Caution should be exercised in patients prone to hypotension and the use of a lower starting dose (0.5 mg b.i.d.) should be considered.

Impaired Liver Function: The pharmacokinetics of risperidone did not change in patients with impaired liver function in response to a 1 mg single dose. However, clinical experience is lacking in these patients. Until further experience is gained, the following dosage schedule is recommended. The starting dose should be 0.5 mg b.i.d. This dosage can be individually adjusted in 0.5 mg b.i.d. increments to 1 to 2 mg b.i.d.

Impaired Kidney Function: Since the pharmacokinetics of risperidone changed substantially in patients with renal disease, even in response to a 1 mg single dose (see Pharmacology, Pharmacokinetics and Precautions), and since to date no clinical experience is available, dosage recommendations cannot be made in this patient population.

Switching from Other Antipsychotics: When medically appropriate, gradual discontinuation of the previous treatment, while risperidone therapy is initiated is recommended. In all cases the period of overlapping antipsychotic administration should be minimized. When switching patients from depot antipsychotics, initiate risperidone therapy in place of the next scheduled injection. The need for continuing existing anti-parkinsonian medications should be re-evaluated periodically.

Oral Solution: Each mL of oral solution contains: risperidone 1 mg as risperidone tartrate. Nonmedicinal ingredients: benzoic acid, purified water, sodium hydroxide and tartaric acid. Bottles of 100 mL with a calibrated (in mg and in mL) pipette. The minimum calibrated volume is 0.25 mL, while the maximum calibrated volume is 3 mL. Store between 15 and 30°C. Protect from light and freezing. Keep out of reach of children. Patient Instructions (including illustrations) for using the Risperdal calibrated dispensing-pipette are provided (see Blue Section - Information for the Patient). Tests indicate that risperidone oral solution is compatible in the following beverages: water, coffee, orange juice and low-fat milk; however, it is not compatible with cola or tea.

Tablets: 1 mg: Each white, film-coated, half-scored, oblong tablet, marked JANSSEN and R 1, contains:

risperidone 1 mg. Nonmedicinal ingredients: colloidal anhydrous silica, hypromellose, lactose, magnesium stearate, maize starch, microcrystalline cellulose, propylene glycol and sodium lauryl sulfate. Blister packages of 60 and HDPE bottles of 250.

2 mg: Each orange, film-coated, oblong tablet, marked JANSSEN and R 2, contains: risperidone 2 mg. Nonmedicinal ingredients: colloidal anhydrous silica, hypromellose, lactose, magnesium stearate, maize starch, microcrystalline cellulose, propylene glycol, sodium lauryl sulfate, sunset yellow (E110) aluminum lake, talc and titanium dioxide (E171). Blister packages of 60 and HDPE bottles of 250.

3 mg: Each yellow, film-coated, oblong tablet, marked JANSSEN and R 3, contains: risperidone 3 mg. Nonmedicinal ingredients: colloidal anhydrous silica, hypromellose, lactose, magnesium stearate, maize starch, microcrystalline cellulose, propylene glycol, quinoline yellow (E104), sodium lauryl sulfate, talc and titanium dioxide (E171). Blister packages of 60 and HDPE bottles of 250.

4 mg: Each green, film-coated, oblong tablet, marked JANSSEN and R 4, contains: risperidone 4 mg. Nonmedicinal ingredients: colloidal anhydrous silica, hypromellose, indigotindisulfonate (E132) aluminum lake, lactose, magnesium stearate, maize starch, microcrystalline cellulose, propylene glycol, quinoline yellow (E104), sodium lauryl sulfate, talc and titanium dioxide (E171). Blister packages of 60 and HDPE bottles of 250.

Store tablets between 15 and 30°C, protected from light and moisture. Keep out of the reach of children.

Long-Term Bipolar I Disorder Treatment

http://www.risperdalconsta.com/ December 09, 2014

Learn about RISPERDAL® CONSTA® (risperidone) and how it can help those living with Bipolar I Disorder. See Safety & full Prescribing Information.

RISPERDAL® CONSTA® (risperidone) is approved for the treatment of schizophrenia and for the maintenance treatment of Bipolar I Disorder.

Elderly Patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death compared to placebo. RISPERDAL® CONSTA® (risperidone) is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS) is a rare and potentially fatal side effect reported with RISPERDAL® CONSTA® and similar medicines. Call your doctor immediately if the person being treated develops symptoms such as high fever; stiff muscles; shaking; confusion; sweating; changes in pulse, heart rate, or blood pressure; or muscle pain and weakness. Treatment should be stopped if the person being treated has NMS.

Tardive Dyskinesia (TD) is a serious, sometimes permanent side effect reported with RISPERDAL® CONSTA® and similar medications. TD includes uncontrollable movements of the face, tongue, and other parts of the body. The risk of developing TD and the chance that it will become permanent is thought to increase with the length of therapy and the overall dose taken by the patient. This condition can develop after a brief period of therapy at low doses, although this is much less common. There is no known treatment for TD, but it may go away partially or completely if therapy is stopped.

Atypical antipsychotic drugs have been associated with metabolic changes that can increase cardiovascular/cerebrovascular risks. These changes may include:

High blood sugar and diabetes have been reported with RISPERDAL® CONSTA® and similar medicines. If you already have diabetes or have risk factors such as being overweight or a family history of diabetes, blood sugar testing should be done at the beginning and during the treatment. The complications of diabetes can be serious and even life-threatening. Call your doctor if you develop signs of high blood sugar or diabetes, such as being thirsty all the time, having to urinate or “pass urine” more often than usual, or feeling weak or hungry.

Changes in cholesterol and triglycerides have been noted in patients taking atypical antipsychotics. Check with your doctor while on treatment.

Weight gain has been reported in patients taking atypical antipsychotics. Monitor weight gain while on treatment.

RISPERDAL® CONSTA® and similar medications can raise the blood levels of a hormone known as prolactin, causing a condition known as hyperprolactinemia. Blood levels of prolactin remain elevated with continued use. Some side effects seen with these medications include the absence of a menstrual period; breasts producing milk; the development of breasts by males; and the inability to achieve an erection.

Some people taking RISPERDAL® CONSTA® may feel faint or lightheaded when they stand up or sit up too quickly. By standing up or sitting up slowly and following your healthcare professional's dosing instructions, this side effect can be reduced or it may go away over time.

Blood problems such as low numbers of white blood cells have been reported in patients taking risperidone and similar medications. In some cases it has been serious and life-threatening. Depending upon your medical condition, your doctor may choose to test your blood as you start therapy with RISPERDAL® CONSTA®.

RISPERDAL® CONSTA® may affect your alertness or driving ability; therefore, do not drive or operate machinery before talking to your healthcare professional.

RISPERDAL® CONSTA® should be used cautiously in people with a seizure disorder, who have had seizures in the past, or who have conditions that increase their risk for seizures.

Painful, long-lasting erections have been reported with the use of RISPERDAL® CONSTA®. Call your doctor immediately if you think you are having this problem.

Extrapyramidal Symptoms (EPS) are usually persistent movement disorders or muscle disturbances, such as restlessness, tremors, and muscle stiffness. If you observe any of these symptoms, talk to your healthcare professional.

Inform your healthcare professional if you become pregnant or intend to become pregnant during therapy with RISPERDAL® CONSTA®. Caution should be used when administering RISPERDAL® CONSTA® to a nursing woman.

RISPERDAL® CONSTA® may make you more sensitive to heat. You may have trouble cooling off, or be more likely to become dehydrated, so take care when exercising or when doing things that make you warm.

Some medications interact with RISPERDAL® CONSTA®. Please inform your healthcare professional of any medications or supplements that you are taking. Avoid alcohol while taking RISPERDAL® CONSTA®.

In a study of people taking RISPERDAL® CONSTA®, the most common side effects in the treatment of schizophrenia were headache, tremors, dizziness, restlessness, tiredness, constipation, indigestion, sleepiness, weight gain, pain in the limbs, and dry mouth.

In a study of people taking RISPERDAL® CONSTA®, the most common side effects in the treatment of bipolar disorder were weight gain (when used alone) and tremors (when used with lithium or valproate).

If you have any questions about RISPERDAL® CONSTA® or your therapy, talk with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

For more information about RISPERDAL® CONSTA®, please read the Important Product Information.

RISPERIDONE - WHO | World Health Organization

http://www.who.int/selection_medicines/committees/expert/19/applications/Risperidone_24_A_Ad_Final.pdf December 09, 2014

3 1. Summary Statement of the Proposal for Inclusion of Risperidone Risperidone, a benzisoxazole derivative atypical antipsychotic medication, is proposed for ...

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Application for Inclusion to the 19th Expert Committee on the
          Selection and Use of Essential Medicines:
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RISPERIDONE

January 6, 2013

Submitted by:

Jasleen Salwan, Hiwot Woldu, M.D., Anna Rosen, M.D., and Craig L. Katz, M.D.

The Mount Sinai School of Medicine

Program in Global Mental Health

New York, New York, USA

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1. Summary Statement of the Proposal for Inclusion of Risperidone

Risperidone, a benzisoxazole derivative atypical antipsychotic medication, is proposed for inclusion in the WHO Model List of Essential Medications for treatment of schizophrenia, mania, and autism. To date, the list of essential medications does not include atypical antipsychotics, which play a critical role in the treatment of psychotic disorders. This application provides a systematic review of the use, efficacy, safety, availability, and cost-effectiveness of risperidone compared with both typical and other atypical antipsychotic medications.

In the United States, risperidone is the most commonly reported atypical antipsychotic medication prescribed. It is approved for use in schizophrenia, mania of bipolar disorder, and irritability and aggression of autism. It is also effectively used in other instances of psychosis, including schizoaffective disorder, depression with psychotic features, and psychosis secondary to general medical conditions, including infectious diseases, and may be effective in other conditions such as major depression, various anxiety disorders including OCD, delirium, dementia and substance abuse disorders. Risperidone is effective for widespread treatment in children, adolescents, adults, and the elderly.

Evidence shows that risperidone is often more effective in the treatment of psychosis than the most commonly prescribed typical psychotic medication, haloperidol, which is included in the current list of WHO essential medications with chlorpromazine and fluphenazine. In multiple studies, risperidone is more likely than haloperidol to improve scores in the Positive and Negative Syndrome Scale (PANSS), reduce relapse rates of psychosis, improve cognitive function in schizophrenia, and improve manic symptoms in bipolar disorder.

Because risperidone has a different side effect profile than typical antipsychotic medications like haloperidol, it provides an essential alternative treatment for those people who cannot tolerate the older medications. Much psychosis may go under-treated because of discontinuation of typical antipsychotics due to side effects. Risperidone has fewer reported extrapyramidal side effects and akathisia than typical antipsychotics, and studies show less mortality associated with risperidone than with haloperidol. Although it is associated with metabolic disturbances, the overall side effect profile of risperidone is encouraging when compared not only with typical antipsychotic medications, but with other medications in its own class. Studies show less weight gain and onset of diabetes than olanzapine and less cholesterol elevation than other atypical antipsychotics.

Risperidone represents a class of medication, atypical antipsychotics, that should be included in the essential medications list. Within its class, the choice of risperidone offers a uniquely good balance of efficacy, safety, minimal monitoring, and cost-effectiveness. Risperidone is an important treatment option that can reduce the global disease burden of psychosis, mania, and autism.

3

2. Focal Point Person(s) in the World Health Organization

Dr. K Weerasuriya, Medical Officer
Medicines Access and Rational Use (MAR)
Essential Medicines and Health Products (EMP)

4

3. Name of the Organization(s) Consulted and Supporting the Application

- Ministry of Health, Belize
- Ministry of Health and the Environment, Saint Vincent/Grenadines
- Sumandeep Vidyapeeth University, Vadadora (Gujarat), India

SEE APPENDIX FOR LETTERS OF SUPPORT

5

4. International Nonproprietary Name (INN, generic name) of the medicine

risperidone

6

5. Formulations of Risperidone Proposed for Inclusion

Core List

- Tablets 0.25 mg, 1 mg, 2 mg

Complementary List

- Oral Solution: 1 mg/mL – 30 mL bottle
- Risperidone long-acting depot microspheres formulation for deep intramuscular administration 25 mg vial/kit

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6. International Availability

Name	Manufacturer	Country	Form
Rispa	Sigma, Austral.	Australia	(Form Not Given)
Risperdal	Janssen-Cilag, Austral.	Australia	(Form Not Given)
Rixadone	Alphapharm, Austral.	Australia	(Form Not Given)
Aleptan	Lannacher, Austria	Austria	(Form Not Given)
Belivon (FM)	Organon, Austria	Austria	(Form Not Given)
Risperdal	Janssen-Cilag, Austria	Austria	(Form Not Given)
Rispolin (FM)	Janssen-Cilag, Austria	Austria	(Form Not Given)
Risperdal	Janssen-Cilag, Belg.	Belgium	(Form Not Given)
Torendo	HCS, Neth.	Belgium	(Form Not Given)
Esquidon	Merck, Braz.	Brazil	(Form Not Given)
Respidon	Torrent, Braz.	Brazil	(Form Not Given)
Ripevil	GSK, Braz.	Brazil	(Form Not Given)
Risleptic	Arrow, Braz.	Brazil	(Form Not Given)
Risperdal	Janssen-Cilag, Braz.	Brazil	(Form Not Given)
Risperix	Aspen, Braz.	Brazil	(Form Not Given)
Riss (DI)	Eurofarma, Braz.	Brazil	(Form Not Given)
Viverdal	Uniao Quimica, Braz.	Brazil	(Form Not Given)
Zargus	Biosintetica, Braz.	Brazil	(Form Not Given)
Risperdal	Janssen-Ortho	Canada	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperdal M-Tab	Janssen-Ortho	Canada	0.5 MG

disintegrating tablet; 1 M

Dagotil	Royal, Chile	Chile	(Form Not Given)
Goval	Pharma Investi, Chile	Chile	(Form Not Given)
Radigen	Medipharm, Chile	Chile	(Form Not Given)
Risperdal	Janssen-Cilag, Chile	Chile	(Form Not Given)
Spiron	Andromaco, Chile	Chile	(Form Not Given)
Apo-Risper	Apotex, Cz.	Czech Republic	(Form Not Given)
Medorisper	Medochemie, Cz.	Czech Republic	(Form Not Given)
Ridoner	ICN, Cz.	Czech Republic	(Form Not Given)
Rileptid	Egis, Cz.	Czech Republic	(Form Not Given)
Risepro	Valeant, Cz.	Czech Republic	(Form Not Given)
Rispen	Zentiva, Cz.	Czech Republic	(Form Not Given)
Rispera	Teva, Cz.	Czech Republic	(Form Not Given)

Risperdal	Janssen-Cilag, Cz.	Czech Republic	(Form Not Given)
Risperigamma (FM)	Worwag, Cz.	Czech Republic	(Form Not Given)
Risperstad (FM)	Stada, Cz.	Czech Republic	(Form Not Given)
Rispolux	Sandoz, Cz.	Czech Republic	(Form Not Given)
Risset (FM)	Pliva, Cz.	Czech Republic	(Form Not Given)
Rorendo	KRKA, Cz.	Czech Republic	(Form Not Given)
Unispera (FM)	Belupo, Cz.	Czech Republic	(Form Not Given)
Ripexal	Hexal, Denm.	Denmark	(Form Not Given)
Risperanne	Sandoz, Denm.	Denmark	(Form Not Given)
Risperdal	Janssen-Cilag, Denm.	Denmark	(Form Not Given)
Rispolept	Abacus, Denm.	Denmark	(Form Not Given)
Rispazin	Leiras, Fin.	Finland	(Form Not Given)
Risperdal	Janssen-Cilag, Fin.	Finland	(Form Not Given)
Risperdal	Janssen-Cilag, Fr.	France	(Form Not Given)
Risperdalconsta	Janssen-Cilag, Fr.	France	(Form Not Given)
Risperdaloro	Janssen-Cilag, Fr.	France	(Form Not Given)
Risocon (DI)	Mibe, Ger.	Germany	(Form Not Given)
Rispenon	Tiefenbacher, Neth.	Germany	(Form Not Given)
Rispe-Q (FM)	Juta, Ger.	Germany	(Form Not Given)
Risperdal	Janssen	Germany	1 MG coated tablet; 2 MG coated
Risperdal	Janssen-Cilag, Ger.	Germany	(Form Not Given)
Risperdoc (FM)	Docpharm, Ger.	Germany	(Form Not Given)
Risperigamma	Worwag, Ger.	Germany	(Form Not Given)
Rispimed	Regiomedica, Neth.	Germany	(Form Not Given)
Rispimed (FM)	Regiomedica, Cz.	Germany	(Form Not Given)
Rispimedica (FM)	Basics, Neth.	Germany	(Form Not Given)
Adovia	Pharmacypria, Gr.	Greece	(Form Not Given)
Axelabron	Ferakon, Gr.	Greece	(Form Not Given)
Belasperdal-S	SJA, Gr.	Greece	(Form Not Given)
Capulton	Farmex, Gr.	Greece	(Form Not Given)
Depolan (DI)	Gap, Gr.	Greece	(Form Not Given)
Depredon	Kleva, Gr.	Greece	(Form Not Given)
Dixine	Lavipharm, Gr.	Greece	(Form Not Given)
Evitrat	Unipharma, Gr.	Greece	(Form Not Given)

Helposper	Help, Gr.	Greece	(Form Not Given)
Isipredon	Heremco, Gr.	Greece	(Form Not Given)

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Lassen	Farmanic, Gr.	Greece	(Form Not Given)
Leterzin	Panagiotis, Gr.	Greece	(Form Not Given)
Lucipral	Balu, Gr.	Greece	(Form Not Given)
Muistin	Verisfield, Gr.	Greece	(Form Not Given)
Nerve	Med-One, Gr.	Greece	(Form Not Given)
Novoris	Novofarm (Novofarm), Gr.	Greece	(Form Not Given)
Orotral	SM, Gr.	Greece	(Form Not Given)
Preridon	Alapis, Gr.	Greece	(Form Not Given)
Psychordal	Viofar, Gr.	Greece	(Form Not Given)
Ribex (DI)	Vianex (Vianex), Gr.	Greece	(Form Not Given)
Rifocus	Gerolymatos, Gr.	Greece	(Form Not Given)
Rigenin (FM)	Labochem, Cz.	Greece	(Form Not Given)
Ripepral	Verisfield, Gr.	Greece	(Form Not Given)
Ripetomar (FM)	Labochem, Cz.	Greece	(Form Not Given)
Risenar	Minerva (Minerva), Gr.	Greece	(Form Not Given)
Risgal	Galenus, Gr.	Greece	(Form Not Given)
Risidral	Pharmanel, Gr.	Greece	(Form Not Given)
Rispadim (FM)	Labochem, Cz.	Greece	(Form Not Given)
Rispalm	Polychronus, Gr.	Greece	(Form Not Given)
Rispedep (FM)	Labochem, Cz.	Greece	(Form Not Given)
Rispedolet (FM)	Labochem, Cz.	Greece	(Form Not Given)
Rispedospes (FM)	Labochem, Cz.	Greece	(Form Not Given)
Rispefar	Specifar, Gr.	Greece	(Form Not Given)
Rispelen	Elpen (Elpen), Gr.	Greece	(Form Not Given)
Rispemar (FM)	Labochem, Cz.	Greece	(Form Not Given)
Rispen	Gabriel, Gr.	Greece	(Form Not Given)
Rispenet	Faran, Gr.	Greece	(Form Not Given)
Risperascol	Alet, Gr.	Greece	(Form Not Given)
Risperdal	Janssen-Cilag, Gr.	Greece	(Form Not Given)
Risperinin (FM)	Labochem, Cz.	Greece	(Form Not Given)
Risperit (FM)	Labochem, Cz.	Greece	(Form Not Given)
Risperom	Integris, Gr.	Greece	(Form Not Given)
Risperoprol	Proel, Gr.	Greece	(Form Not Given)
Rispersan	Santa, Gr.	Greece	(Form Not Given)
Rispogen	Genepharm, Gr.	Greece	(Form Not Given)
Sperelax	Biospray, Gr.	Greece	(Form Not Given)
Wisperdon	Proton, Gr.	Greece	(Form Not Given)
Zafitral	Rafarm, Gr.	Greece	(Form Not Given)
Rileptid	Egis, Hong Kong	Hong Kong	(Form Not Given)

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Risperdal	Janssen, Hong Kong	Hong Kong	(Form Not Given)
Risperigamma	Worwag, Hong Kong	Hong Kong	(Form Not Given)
Hunperdal	Gedeon Richter, Hung.	Hungary	(Form Not Given)
Perdox	Vera, Hung.	Hungary	(Form Not Given)
Rileptid	Egis, Hung.	Hungary	(Form Not Given)
Ripedon	Solamed, Hung.	Hungary	(Form Not Given)
Rispe	Ratiopharm, Hung.	Hungary	(Form Not Given)
Risperdal	Janssen-Cilag, Hung.	Hungary	(Form Not Given)
Rispolux	Sandoz, Hung.	Hungary	(Form Not Given)
Rispons	Actavis, Hung.	Hungary	(Form Not Given)
Ronkal (FM)	Zentiva, Hung.	Hungary	(Form Not Given)
Rosipin	Medico Uno, Hung.	Hungary	(Form Not Given)
Torendo	KRKA, Hung.	Hungary	(Form Not Given)
Ziperid	Valeant, Hung.	Hungary	(Form Not Given)
Neripros	Pharos, Indon.	Indonesia	(Form Not Given)
Nodiril	Actavis, Indon.	Indonesia	(Form Not Given)
Persidal	Mersifarma, Indon.	Indonesia	(Form Not Given)
Risperdal	Alkermes, Indon.	Indonesia	(Form Not Given)
Rizodal	Guardian, Indon.	Indonesia	(Form Not Given)
Zofredal	Kalbe, Indon.	Indonesia	(Form Not Given)
Perdamel	Clonmel, Irl.	Ireland	(Form Not Given)
Resdal (FM)	Niche, Irl.	Ireland	(Form Not Given)
Rispal	Pinewood, Irl.	Ireland	(Form Not Given)
Rispatal	Chanelle, Irl.	Ireland	(Form Not Given)
Risperdal	Janssen-Cilag, Irl.	Ireland	(Form Not Given)
Risperger	Gerard, Irl.	Ireland	(Form Not Given)
Rispone	Rowex, Irl.	Ireland	(Form Not Given)
Risperdal	Janssen-Cilag, Israel	Israel	(Form Not Given)
Risperidex	Dexcel, Israel	Israel	(Form Not Given)

Rispond	Trima, Israel	Israel	(Form Not Given)
Speridone	Tedec Meiji, Israel	Israel	(Form Not Given)
Belivon	JC Healthcare, Ital.	Italy	(Form Not Given)
Risperdal	Janssen-Cilag, Ital.	Italy	(Form Not Given)
Risperdal	Janssen, Jpn	Japan	(Form Not Given)
Risperdal	Janssen-Cilag, Malaysia	Malaysia	(Form Not Given)
Rozidal	Ranbaxy, Malaysia	Malaysia	(Form Not Given)
Limbik	Psicofarma, Mex.	Mexico	(Form Not Given)
Reskizof	Pisa, Mex.	Mexico	(Form Not Given)
Risperdal	Janssen-Cilag, Mex.	Mexico	(Form Not Given)

Rispolux	Sandoz, Mex.	Mexico	(Form Not Given)
Silderec	Probiomed, Mex.	Mexico	(Form Not Given)
Upmotev	Teva, Mex.	Mexico	(Form Not Given)
Belivon (FM)	Janssen-Cilag, Neth.	Netherlands	(Form Not Given)
Risperdal	Janssen-Cilag, Neth.	Netherlands	(Form Not Given)
Ridal	Douglas, NZ	New Zealand	(Form Not Given)
Risperdal	Janssen-Cilag, NZ	New Zealand	(Form Not Given)
Risperon	Mylan, NZ	New Zealand	(Form Not Given)
Risperdal	Janssen-Cilag, Norw.	Norway	(Form Not Given)
Aspidon	Torrent, Philipp.	Philippines	(Form Not Given)
Renuvie	Medichem, Philipp.	Philippines	(Form Not Given)
Rileptid	Egis, Philipp.	Philippines	(Form Not Given)
Risdin	MedChoice, Philipp.	Philippines	(Form Not Given)
Rispedin	Shine, Philipp.	Philippines	(Form Not Given)
Risperdal	Janssen, Philipp.	Philippines	(Form Not Given)
Rispond	Brown & Burk, Philipp.	Philippines	(Form Not Given)
Apo-Risperid	Apotex, Pol.	Poland	(Form Not Given)
Disaperid	Biogened, Pol.	Poland	(Form Not Given)
Doresol	Jelfa, Pol.	Poland	(Form Not Given)
Galperinon	Galena, Pol.	Poland	(Form Not Given)
Lioxam (FM)	Grunenthal, Pol.	Poland	(Form Not Given)
Mepharis (FM)	Mepha, Pol.	Poland	(Form Not Given)
Nodir	Polfarmex, Pol.	Poland	(Form Not Given)
Orizon	Orion, Pol.	Poland	(Form Not Given)
Ranperidon	Ranbaxy, Pol.	Poland	(Form Not Given)
Rispen	Zentiva, Pol.	Poland	(Form Not Given)
Risperatio (FM)	Ratiopharm, Pol.	Poland	(Form Not Given)
Risperiwin (FM)	Winthrop, Pol.	Poland	(Form Not Given)
Risperon	Lek-Am, Pol.	Poland	(Form Not Given)
Rispofren (FM)	Biofarm, Pol.	Poland	(Form Not Given)
Rispolept	Janssen-Cilag, Pol.	Poland	(Form Not Given)
Rispolux	Sandoz, Pol.	Poland	(Form Not Given)
Risset	Farmacom, Pol.	Poland	(Form Not Given)
Ryspolit	Polpharma, Pol.	Poland	(Form Not Given)
Speridan	Actavis, Pol.	Poland	(Form Not Given)
Torendo	KRKA, Pol.	Poland	(Form Not Given)
Ziperid	ICN, Pol.	Poland	(Form Not Given)
Belivon (FM)	Janssen-Cilag, Port.	Portugal	(Form Not Given)
Itraxel	Normal, Port.	Portugal	(Form Not Given)

Lergitec	Atral, Port.	Portugal	(Form Not Given)
Lotin (DI)	Pentafarma, Port.	Portugal	(Form Not Given)
Perdin	Merck, Port.	Portugal	(Form Not Given)
Ripax (DI)	KRKA, Port.	Portugal	(Form Not Given)
Risperdal	Janssen, Port.	Portugal	(Form Not Given)
Smissen (FM)	Cinfa, Port.	Portugal	(Form Not Given)
Zoridal	Decomed, Port.	Portugal	(Form Not Given)
Ridal	Douglas, Singapore	Singapore	(Form Not Given)
Risperdal	Janssen-Cilag, Singapore	Singapore	(Form Not Given)
Perizal	Specpharm, S.Afr.	South Africa	(Form Not Given)
Risperdal	Janssen-Cilag, S.Afr.	South Africa	(Form Not Given)
Risperlet	Janssen-Cilag, S.Afr.	South Africa	(Form Not Given)
Risponz	Zydus, S.Afr.	South Africa	(Form Not Given)
Zoxadon	Pharma Dynamics, S.Afr.	South Africa	(Form Not Given)
Arketin	Qualigen, Spain	Spain	(Form Not Given)
Atornil (FM)	Ferrer, Spain	Spain	(Form Not Given)
Diaforin	Brainpharma, Spain	Spain	(Form Not Given)
Neclav (DI)	Farmalider, Port.	Spain	(Form Not Given)
Risfarmal (FM)	Brainpharma, Spain	Spain	(Form Not Given)
Rispemylan	Mylan, Spain	Spain	(Form Not Given)
Risperdal	Janssen-Cilag, Spain	Spain	(Form Not Given)

Risperdal	Janssen-Cilag, Swed.	Sweden	(Form Not Given)
Risperdal	Janssen-Cilag, Switz.	Switzerland	(Form Not Given)
Risperdal	Janssen-Cilag, Thai.	Thailand	(Form Not Given)
Nodirep	Bio-Gen, Turk.	Turkey	(Form Not Given)
Perilife	Frik, Turk.	Turkey	(Form Not Given)
Restela	Deva, Turk.	Turkey	(Form Not Given)
Ricus	Biofarma, Turk.	Turkey	(Form Not Given); (Form Not G
Ripesil	Ali, Turk.	Turkey	(Form Not Given)
Risperdal	Janssen-Cilag, Turk.	Turkey	(Form Not Given)
Rixol	Bilim, Turk.	Turkey	(Form Not Given)
Rixper	Fako, Turk.	Turkey	(Form Not Given)
Neirispin	Zdorovje, Ukr.	Ukraine	(Form Not Given)
Ridonex	Gedeon Richter, Ukr.	Ukraine	(Form Not Given)
Rileptid (FM)	Egis, Ukr.	Ukraine	(Form Not Given)
Risperon	Interfarma, Ukr.	Ukraine	(Form Not Given)
Risset	Pliva, Ukr.	Ukraine	(Form Not Given)
Risperdal	Janssen-Cilag, UK	United Kingdom	(Form Not Given)

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Rispeva	Teva, Irl.	United Kingdom	(Form Not Given)
Risperdal	Janssen Pharmaceuticals	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperdal	Janssen, USA	United States	(Form Not Given)
Risperdal Consta	Janssen Pharmaceuticals	United States	12.5 MG Powder for Suspension
Risperdal M-Tab	Janssen Pharmaceuticals	United States	0.5 MG Tablet, Disintegrating; 1
Risperidone	Amneal Pharmaceuticals	United States	1 MG/ML Solution
Risperidone	Apotex	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Apotex (Canada)	United States	1 MG/ML Solution
Risperidone	Aurobindo Pharma	United States	1 MG/ML Solution
Risperidone	Aurobindo Pharma (India)	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Aurolife Pharma	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Barr Laboratories	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	BayPharma	United States	1 MG/ML Solution
Risperidone	Bio-Pharm	United States	1 MG/ML Solution
Risperidone	Dr Reddy's Laboratories	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Gen-Source RX	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Jubilant Cadista Pharmaceuticals	United States	0.5 MG Tablet, Disintegrating; 1
Risperidone	Mylan Pharmaceuticals	United States	0.5 MG Tablet; 0.5 MG Tablet, D Tablet, Disintegrating
Risperidone	Par Pharmaceutical	United States	0.5 MG Tablet, Disintegrating; 0.
Risperidone	Patriot Pharmaceuticals	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Qualitest Pharmaceuticals	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Roxane Laboratories	United States	1 MG/ML Solution
Risperidone	Sandoz	United States	0.5 MG Tablet, Disintegrating; 1
Risperidone	Teva Pharmaceuticals	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Torrent Pharma	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Watson Laboratories	United States	0.5 MG Tablet; 0.25 MG Tablet; 1
Risperidone	Wockhardt (India)	United States	1 MG/ML Solution

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Risperidone 0.5 MG Tablet; 0.25 MG Tablet; 1	Wockhardt USA	United States
Risperidone 0.5 MG Tablet; 0.25 MG Tablet; 1	Zydus Pharmaceuticals	United States
Risperidone M-TAB 0.5 MG Tablet, Disintegrating; 1	Patriot Pharmaceuticals	United States
Risperidone ODT 0.5 MG Tablet, Disintegrating; 1	Dr Reddy's Laboratories	United States
Risperidone ODT 0.5 MG Tablet, Disintegrating; 1	Zydus Pharmaceuticals	United States
Ridal (Form Not Given)	Giempi, Venez.	Venezuela
Risperdal (Form Not Given)	Janssen-Cilag, Venez.	Venezuela
Risperid (Form Not Given)	Roemmers, Venez.	Venezuela

Sources

The above information was obtained from the following international drug name databases:

Lexi-Comp ONLINE
Micromedex

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7. Listing for risperidone is requested as an individual medication.

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8. Information Supporting the Public Health Relevance of Risperidone

Antipsychotics have been shown to be efficacious in treating a range of mental illnesses, including schizophrenia and bipolar disorder in both adults and youth (Leucht, Heres, Kissling, & Davis, 2011) (Malhi, Adams, Cahill, Dodd, & Berk, 2009) (Correll, Kratochvil, & March, 2011) (Pfeifer, Kowatch, & DelBello, 2010), major depressive disorder in adults (Pae, Forbes, & Patkar, 2011) (Anderson et al., 2008) and Tourette syndrome and irritability associated with autism disorders in youth (Pfeifer et al., 2010). At $16.1 billion a year, antipsychotics comprise the fifth-largest share of the U.S. prescription market by spending (IMS, 2012), and its market is growing. In 2008, antipsychotics were used for specific indications in 14.3 million outpatient visits in the U.S., up from 6.2 million in 1995 (Alexander, Gallagher, Mascola, Moloney, & Stafford, 2011).

Atypical, or second-generation, antipsychotics have traditionally been distinguished from typical (first-generation) antipsychotics based on their comparatively minimal association with extra-pyramidal symptoms (Farah, 2005) (Markowitz, Brown, & Moore, 1999). However, at present, the medical community has not reached a consensus on the definition of atypicality (Farah, 2005). Among the various definitions that have emerged, salient characteristics include efficacy in treating both the positive and negative symptoms of schizophrenia (Farah, 2005) (B J Kinon & Lieberman, 1996), efficacy in treating schizophrenic patients unresponsive to traditional antipsychotics (Goldstein, 2000), and reduced ability to cause prolactin elevation (Goldstein, 2000).

Risperidone is a benzisoxazole derivative atypical antipsychotic indicated for treatment of schizophrenia, bipolar mania, and irritability associated with autistic disorder (Pharmaceuticals, 2012). It is both effective and widely prescribed (Farah, 2005). Among the second-generation antipsychotics, risperidone conforms the least to the atypicality criteria (Farah, 2005). EPS and tardive dyskinesia have been reported in the literature (Rosebush & Mazurek, 1999) (Bassitt & de Souza Lobo Garcia, 2000), as has persistent elevation of prolactin levels relative to other atypical (Bruce J Kinon, Gilmore, Liu, & Halbreich, 2003). That said, other research has shown risperidone to reduce the risks of EPS relative to haloperidol (Schillevoort, Boer, Herings, & Roos, 2001).

The mental disorders that risperidone is approved to treathave a high global disease burden. As of 2000, 12% of the world's disability-adjusted life years, or years of life lost due to disability, illness, or premature death, was attributable to mental and neurological disorders; this figure is projected to increase to 15% by 2020 (World Health Organization, 2000). Schizophrenia alone accounts for 2.6% of total DALYs in people aged 15-44 and is the 8th leading cause of DALYs for that age group; bipolar affective disorder, the 9th leading cause, accounts for 2.5% (World Health Organization, 2000). While autism is not among the leading causes of worldwide DALYs listed by the WHO, it has been estimated to have a prevalence rate of 0.64% in Europe within the age range of birth through early adulthood (Wittchen et al., 2011).

In developing countries, between 76% and 85% of people with serious mental illness receive no services (The WHO World Mental Health Survey Consortium, 2004). Even in the developed world, approximately half of people with severe mental disorders go untreated (Wang et al., 2007).

In the U.S., risperidone is among the most commonly reported atypical antipsychotic drugs. In 2008, it was used for specific indications in over 12 million outpatient visits (Alexander et al., 2011). In a prospective, observational review of prescription practices for schizophrenia in 27 countries spanning 4 continents (N=5836), risperidone was among the most frequently prescribed antipsychotic monotherapies, second only to olanzapine (Dossenbach et al., 2008). Similarly, in one study of first-hospitalized patients with bipolar disorder in the Cincinnati, Ohio area of the United States (n=58), risperidone and olanzapine were the most frequently prescribed atypical antipsychotics (Fleck, Hendricks, DelBello, & Strakowski, 2002). In the U.S., 71% of bipolar disorder patients are treated with atypical antipsychotics (Ventimiglia, Kalali, & McIntyre, 2009).

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The target population for risperidone includes children and adolescents as well as adults. From 2003-2004, risperidone was the most frequently prescribed antipsychotic agent in the U.S. outpatient setting for patients under 20 years of age (Aparasu & Bhatara, 2007). Risperidone accounted for 43.81% of outpatient visits involving antipsychotics in that age group, while atypical agents overall comprised 99% of children and adolescent outpatient visits involving antipsychotics (Aparasu & Bhatara, 2007). More broadly, atypical antipsychotics are increasingly being used to treat diverse patient groups, including elderly nursing home residents as well as both publicly and privately insured children and adolescents (Crystal, Olfson, Huang, Pincus, & Gerhard, 2009).

We evaluate the appropriateness of current prescription practices of risperidone in the Comparative Effectiveness section, drawing comparisons to typical and other atypical antipsychotics. Overall, we find risperidone to be advantageous in treating schizophrenia, mania, and autism.

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9. Treatment Details for Risperidone

9.1 Dosing and Duration

Risperidone Dosage Forms (Stahl, 2011), (FDA, 2012)
- Tablets 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 6mg
- Orally disintegrating tablets 0.5 mg, 1 mg, 2 mg
- Oral Solution: 1 mg/mL – 30 mL bottle
- Risperidone long-acting depot microspheres formulation for deep intramuscular administration 25 mg vial/kit, 37.5 mg vial/kit, 50 mg vial/kit

Usual Dosage Range (Stahl, 2011)
- Acute psychosis and bipolar disorder: 2 –8 mg/day orally
- Children and elderly: 0.5–2.0 mg/day orally
- Long-acting depot: 25–50mg every 2 weeks intramuscularly

Dosage Guidelines for Oral Formulations of Approved Uses of Risperidone

Risperidone has US Food and Drug Administration (FDA)-approved uses for schizophrenia, mania associated with bipolar disorder, and irritability associated with autistic disorder.

Unless otherwise noted, oral risperidone may be administered on a once daily or twice daily schedule.

	Initial Dose	Titration	Target Dose	Effective Dose
Schizophrenia/Psychosis in non-emergent settings- Adults	1mg/day in 2 divided doses	1mg daily	4-8 mg daily	4-16 mg /day
Schizophrenia- Adolescents	0.5mg/day	0.5-1mg daily	3mg/day	1-6mg/day
Bipolar Mania- Adults	2-3mg/day	1mg daily	1-6mg/day	1-6mg/day
Bipolar Mania in children/adolescents	0.5mg/day	0.5 – 1mg daily	2.5mg/day	0.5–6mg/day
Irritability associated with autistic disorder	0.25mg/day (<20kg) 0.5mg/day (≥20 kg)	0.25-0.5mg at ≥ 2 weeks	0.5 mg /day (<20 kg) 1 mg /day (≥20 kg)	0.5-3mg /day

(Stahl, 2011), (FDA, 2012)

Similar to the FDA, the European Medicines Agency (EMA), the Medicines and Healthcare Products Regulatory Agency (MHRA) of the United Kingdom, and the Australian Therapeutic Goods Administration (TGA), all have approved uses for risperidone in schizophrenia, mania associated with bipolar disorder, and behavioral disturbance in children and adolescents associated with autism and conduct disorder. The recommended doses and age ranges are similar to the FDA guidelines listed in the above table. The EMA, MHRA and TGA also approve the short-term use of risperidone in treating persistent aggression in patients with moderate to severe Alzheimer's dementia when there is risk of harm to self or others and the aggression is refractory to non-pharmacological approaches (MHRA, 2011 & 2006), (EMA, 2008), (TGA, 2010, '05, '04, '02, 1999).

Dosage Guidelines for Long-Acting Formulation of Risperidone
(Stahl, 2011)

Long –acting risperidone is not recommended for patients that have not already demonstrated tolerability to oral risperidone.

	Initial Dose	Titration	Target Dose	Effective Dose
Long-acting Risperidone	25mg intramuscular gluteal injection every 2 weeks.*	At >4weeks	25-50mg IM every 2 weeks	25-50mg IM every 2 weeks

* Onset of action when initiating long-acting risperidone may be delayed for 2 weeks. If a patient is on an oral antipsychotic at initiation of long-acting risperidone, oral antipsychotic should be continued for 3 more weeks. If a patient is not on oral antipsychotics at initiation of long-acting risperidone formulation, oral antipsychotic medication should be given with the first injection of the long-acting risperidone and continued for 3 weeks thereafter.

For missed long-acting risperidone injections 2 or more weeks late (i.e., 28 or more days following last injection), antipsychotic coverage may be needed with oral administration for 3 weeks while reinitiating injections

The Australian Therapeutic Goods Administration (TGA), European Medicines Agency (EMA), and Medicines and Healthcare Products Regulatory Agency (MHRA) all approve the use of long-acting risperidone in schizophrenia and other psychotic disorders with dosing similar to those of the FDA outlined in the table above (TGA, 2010), (EMA, 2008) (MHRA, 2008)

Special Populations
(Stahl, 2011), (FDA, 2012)

Pediatric Use of Risperidone:

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Schizophrenia: safety and effectiveness not established for less than 13 years of age
Bipolar Mania: safety and effectiveness not established for less than 10 years of age
Autistic Disorder: safety and effectiveness not established for less than 5 years of age.

Children and elderly may need to have oral twice daily dosing during initiation and titration of risperidone and then can switch to oral once daily when maintenance dose is reached. Dosage increases in this patient population should be in increments of no more than 0.5mg twice daily.

Children and the elderly may require twice daily dosing during initiation and titration of risperidone dosing and can then be switched to oral once daily dosing once maintenance dose is reached.

Pregnancy:
Risperidone is in pregnancy risk category C (there are no controlled studies in humans, but some animal studies show adverse effects].

Patients on risperidone should be counseled about the risks and benefits of breastfeeding.

Pharmacokinetics
(Stahl, 2011), (FDA, 2012)

Risperidone is metabolized by CYP450 2D6 and has active metabolites.

- Parent drug of oral formulation: 20—24 hour half-life
- Long-acting risperidone: 3—6 day half-life
- Long-acting risperidone has elimination phase of approximately 7—8 weeks after last injection

Onset of Action
(Stahl, 2011)
Improvement in psychotic as well as manic symptoms can occur within 1 week, but full effect on cognition, behavior, and affective stabilization may take several weeks. Four to six weeks wait is generally recommended to determine efficacy of

risperidone. However, some patients may require up to 16 – 20 weeks for improvement of cognitive symptoms.

Long-Term Use
(Stahl, 2011), (FDA, 2012)
Risperidone is FDA approved to delay relapse in long-term treatment of schizophrenia. It is also often used for long-term
maintenance in bipolar disorder and various behavioral disorders.

Overdose
(Stahl, 2011), (FDA, 2012)
Monotherapy overdose of risperidone is rarely lethal. Acute overdose symptoms often are exaggeration of the medication's
known pharmacological effects i.e., tachycardia, hypotension, sedation as well as possible convulsions and difficulty breathing.

Dependence or Abuse
(Stahl, 2011), (FDA, 2012)
None known. Has not been systematically studied in animals or humans.

Discontinuation
(Stahl, 2011)
Rapid oral discontinuation of risperidone may lead to worsening of symptoms and rebound psychosis. A slow tapering over 6 –
8 weeks is recommended for oral formulation especially when cross-titrating with another antipsychotic.

Storage and Handling of Risperidone
(Stahl, 2011), (FDA, 2012)

Tablets- store at controlled room temperature 15°-25°C (59°-77°F). Protect from moisture and light.

Orally disintegrating tablets - store at controlled room temperature 15°-25°C (59°-77°F). Protect from moisture and light.

Oral Solution - store at controlled room temperature 15°-25°C (59°-77°F). Protect from moisture and light.

Risperidone long-acting depot microspheres formulation for deep intramuscular administration- must be kept refrigerated.

9.2 Reference to Risperidone in Existing WHO & other Clinical Guidelines

From the treatment of psychosis section of the World Health Organization's, mhGAP Intervention Guide for mental,
neurological and substance use disorders in non-specialized health settings:
"If the response is inadequate to more than one antipsychotic medication using one medicine at a time at adequate dosage for
adequate duration… Consider second-generation antipsychotics (with the exception of clozapine), if cost and availability is not a
constraint, as an alternative to haloperidol or chlorpromazine" (WHO, 2010).

The American Psychiatric Association's Practice Guideline for Schizophrenia lists risperidone, along with olanzapine,
quetiapine, ziprasidone and aripiprazole, as first line treatment for a first episode of acute phase schizophrenia. Atypical
antipsychotics are also recommended for maintenance treatment of chronic schizophrenia (American Psychiatric Association,
2004). More recent American Psychiatric Association practice guidelines for schizophrenia are not available at the time of this
application.

The American Psychiatric Association's Practice Guideline for t he Treatment of Psychi at ri c Di sorders lists risperidone as consistently efficacious in the treatment of positive symptoms and global psychopathology as well as in increasing the likelihood of clinical response in acutely relapsed patients. Risperidone is also noted to be superior to haloperidol in the prevention of relapse during the maintenance phase of treatment (American Psychiatric Association, 2006).

Schizophrenia treatment guidelines for United Kingdom's The National Institute for Health and Clinical Excellence recommend both typical and atypical antipsychotics as first line for acute and maintenance treatment with the medication decision to be based largely on tolerability and side-effect profile. The only exception is clozapine, which is reserved for treatment-resistant schizophrenia (National Institute for Health and Clinical Excellence, 2009).

9.3 Need for Special Diagnostics, Treatment or Monitoring Facilities and Skills When Prescribing Risperidone

Prior to initiating risperidone therapy (Stahl, 2011), (FDA, 2012)
Obtain baseline weight, waist circumference, blood pressure, fasting plasma glucose and fasting lipid profile.

Monitoring while on risperidone therapy (Stahl, 2011), (FDA, 2012)
- Body Mass Index (BMI) measurements monthly for the first 3 months, then quarterly.
- Blood pressure, fasting lipids, fasting plasma glucose should be evaluated within 3 months and then annually. Monitor earlier and more frequently for patients with diabetes or who have gained >5% of initial weight.
- Patients with low white blood cell count (WBC) or history of drug-induced leucopenia/neutropenia should have complete blood count (CBC) monitored frequently during the first few months, and risperidone should be discontinued if there is a decline of WBC in the absence of other causative factors. Treatment should be suspended if absolute neutrophil count falls below 1,000/mm3.
- There is a rare, but life-threatening onset of diabetic ketoacidosis associated with atypical antipsychotics, which requires immediate treatment. Providers should educate patients and be vigilant about rapid onset of polyuria, polydipsia, weight loss, nausea, vomiting, dehydration, rapid respiration, weakness and clouding of sensorium, even coma.

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10. Summary of the Comparative Effectiveness of Risperidone in a Variety of Clinical Settings

10.1. Identification of Clinical Evidence Regarding Risperidone

A systematic review was conducted using PubMed and Cochrane databases (last search September 2012). These catalogues were searched for articles using keywords “risperidone” and “comparison” for PubMed and “risperidone” only for the Cochrane database search. Further data was obtained through cross-referencing and a hand search of relevant literature. There were no specifications on language.

A total of 541 abstracts in PubMed and 49 reviews in Cochrane databases were identified initially. Among these, 197 were relevant to comparative effectiveness for risperidone. Of the 197 relevant articles, 101 were excluded due to poor study design, small sample size, type of article (e.g. letter to the editor), and/or incomplete or non-available data. As a result, 96 studies and review articles were included in this summary.

10.2. Summary of Available Data on Risperidone

Psychosis:

Comparison with typical (first-generation) antipsychotic medications:

In the most recent Cochrane review comparing risperidone versus typical antipsychotics (Hunter, Joy, Kennedy, Gilbody, & Song, 2003), nine randomized controlled trials (RCT) (n=2368) showed that risperidone was more likely to produce an improvement in the Positive and Negative Syndrome Scale (PANSS) in the short term when compared to Haloperidol. Two randomized controlled trials (n=859) showed similar superior improvement with risperidone in the long term as well. In a smaller two year outcomes study, risperidone and haloperidol exhibited similar efficacy in maintenance treatment of schizophrenia, but the patients on risperidone reported less anxiety and depressive symptoms (Marder et al., 2003). In another study, risperidone showed significantly superior PANSS scores compared to haloperidol, perphenazine and zuclopenthixol (Glick, Shkedy, & Schreiner, 2006). Although chlorpromazine is one of the most widely used typical antipsychotic medications worldwide and is included in the List of Essential Medications, there are no well-designed studies that compare chlorpromazine with risperidone at the time of this proposal. As for the third antipsychotic medication on the current list of essential medications, fluphenazine, we are aware of one study in which patients were switched from either oral haloperidol or fluphenazine to risperidone and were found to have improved symptoms and a reduced side-effect burden (Popovic et al., 2011)

In one RCT (N= 367), risperidone was found to reduce relapse at one-year follow up compared to haloperidol. Risperidone was associated with a lower attrition rate in studies for both short-term (N=3066, 16 RCTs) and long-term trials (N: 1270, 4 RCTs) (Hunter et al., 2003). A double-blind prospective study at 40 sites revealed patients on risperidone have a lower risk of relapse than those treated with haloperidol (Csernansky, Mahmoud, & Brenner, 2002). A naturalistic study with 4,783 participants also found that patients on risperidone or olanzapine monotherapy were less likely to experience relapse than those treated with haloperidol (Dossenbach et al., 2005).

Risperidone is associated with more significant and wide-ranging improvements in cognitive functioning compared to haloperidol (Gallhofer, Bauer, Lis, Krieger, & Gruppe, 1996; Green et al., 1997; Harvey, Rabinowitz, Eerdekens, & Davidson, 2005). With regards to long-term memory dysfunction, risperidone is associated with marginally superior efficacy compared to typical antipsychotic medications (Thornton, Van Snellenberg, Sepehry, & Honer, 2006). The relative superiority of risperidone on spatial working memory performance compared to haloperidol is likely due to the impairments in spatial working memory associated with benztropine, which was used more frequently with patients on haloperidol (McGurk et al., 2004).

Oral risperidone administered with lorazepam was found to be as effective as intramuscular treatment with haloperidol and lorazepam for acute psychotic agitation (Currier et al., 2004). Risperidone and olanzapine monotherapy showed similar efficacy as haloperidol in acute reduction of psychotic symptoms in children (Sikich, Hamer, Bashford, Sheitman, & Lieberman, 2004).

Comparison with other atypical (second-generation) antipsychotic medications:

In a Cochrane review that included 45 blinded randomized controlled trials (n=7760) comparing risperidone versus other atypical antipsychotics, risperidone improved the PANSS total score slightly more than quetiapine (9 RCTs, n=1953) and ziprasidone (3 RCTs, n=1016) but slightly less than olanzapine (15 RCTs, n= 2390) (Komossa et al., 2011). The minimal difference in efficacy between atypical antipsychotics is also reflected in other studies (Addington et al., 2009; Klemp et al., 2011; Malla et al., 2004; McEvoy et al., 2007; Miller et al., 2008; Mullen, Jibson, & Sweitzer, 2001; Robinson et al., 2006; Sauriol et al., 2001; Sikich et al., 2008; Zhang et al., 2011; Zhong, Sweitzer, Hamer, & Lieberman, 2006). A double-blind RCT and a naturalistic study with 1901 participants showed slight advantage in efficacy with risperidone compared to olanzapine (Conley & Mahmoud, 2001; Kasper, Rosillon, & Duchesne, 2001). Contrary to these studies, a double blind comparison between olanzapine versus risperidone reported slight efficacy advantage in favor of olanzapine (Tran et al., 1997).

In a Cochrane review comparing risperidone versus olanzapine for schizophrenia (Jayaram & Hosalli, 2005), both medications were found to be equally effective (2 RCTs, n = 552). One randomized controlled study (n=279) reported better outcome with olanzapine for re-hospitalization and relapse by 12 months (Soares-Weiser, Béchard-Evans, Howard Lawson, Davis, & Ascher-Svanum, 2012), a finding that was also observed in a retrospective comparison of risperidone and olanzapine (Sethuraman, Taylor, Enerson, & Dunayevich, 2005). Clozapine has also been associated with a significantly lower re-hospitalization risk compared to risperidone (Tiihonen et al., 2011) and has also been associated with consistent superiority in efficacy compared to typical antipsychotics followed by olanzapine and risperidone (Citrome, 2012). A meta-analysis of time to all-cause treatment discontinuation showed favorable results for olanzapine versus risperidone (Soares-Weiser et al., 2012). A lower dropout rate for olanzapine compared to risperidone was also observed in a multi-center study (Pelagotti, Santarlasci, Vacca, Trippoli, & Messori, 2004). However, the greater adherence to olanzapine treatment might be associated with the dose frequency of the medication rather than any inherent superiority in efficacy or tolerability of olanzapine (Diaz, Neuse, Sullivan, Pearsall, & Woods, 2004).

A treatment response trajectory from the CATIE chronic schizophrenia trial found that olanzapine treated patients were more likely to stay in the trajectory of responders compared to other atypical antipsychotics including risperidone (Levine, Rabinowitz, Faries, Lawson, & Ascher-Svanum, 2012). Maintaining remission for 6 months was highest with olanzapine followed by quetiapine, perphenazine, ziprasidone and risperidone groups (Levine, Rabinowitz, Ascher-Svanum, Faries, & Lawson, 2011).

These findings were not reflected in a smaller randomized, controlled trial where remission rate did not significantly differ between haloperidol, risperidone, and olanzapine (Crespo-Facorro et al., 2011).

There is some evidence for cognitive improvement after treatment with atypical antipsychotic medications in early psychosis. In a randomized double-blind 52-week comparison, risperidone, quetiapine and olanzapine were all associated with significant

improvements in neurocognition with no significant difference in efficacy between medications (Keefe et al., 2007). Another study found that cognitive improvement with atypical antipsychotics might be due to practice effects such as familiarity and procedural learning. No significant difference in improvement of cognition was found between olanzapine and risperidone in this study either (Goldberg et al., 2007). Quetiapine showed similar efficacy as risperidone in neuropsychological performance and social competence (Harvey, Patterson, Potter, Zhong, & Brecher, 2006; Zhong et al., 2006). A small study found slight neurocognitive advantages with paliperidone ER compared to risperidone (Kim et al., 2012).

A review of antipsychotic use in children and young adults found second-generation antipsychotics improved clinical global impressions and diminished positive and negative symptoms in schizophrenia. There was not a significant difference n efficacy between individual atypical antipsychotics (Seida et al., 2012).

Comparison with Placebo:

In a Cochrane review comparing risperidone versus placebo (Rattehalli, Jayaram, & Smith, 2010), risperidone showed 20% greater reduction in Brief Psychiatric Rating Scale (BPRS)/PANSS score than placebo in seven randomized controlled trails (n = 856), and fewer participants on risperidone needed an additional psychotropic during the trial period (1 RCT, n=186). Placebo and risperidone showed similar Clinical Global Impressions (CGI) global scores in 3 RCTs (n=397). Placebo arm had lower attrition rate (10 RCTs, n=1363), but fewer participants left the trial in the risperidone arm due to lack of efficacy (5 RCTs, n = 888).

Comparison of risperidone long-acting injection with typical and atypical antipsychotic medications:

Risperidone long-acting injection (RLAI) showed rates of symptomatic remission as well as psychosocial improvement comparable to intramuscular long-acting typical antipsychotics, and both classes were significantly more efficacious than Per-os (PO) formulations (Barak & Aizenberg, 2012). Long-acting risperidone was also associated with lower rates of hospitalization (Grimaldi-Bensouda et al., 2012; Tiihonen et al., 2011) but did not have an effect on treatment adherence in first-episode schizophrenia patients (Weiden et al., 2009). RLAI showed superior efficacy compared to paliperidone palmitate (Fleischhacker et al., 2012).

Bipolar Disorder:

A Cochrane review of acute mania identified six trials (n=1343) examining risperidone as monotherapy or in combination with lithium or an anticonvulsant (Jennifer M Rendell, Gijsman, Bauer, Goodwin, & Geddes, 2006). Risperidone was found to be effective in reducing manic symptoms comparable in efficacy to haloperidol.

Comparison with other medications:

A double blind randomized controlled trial found that risperidone, lithium and haloperidol all have equivalent efficacy in the management of acute mania (Segal, Berk, & Brook, 1998). There does not seem to be any difference between risperidone and

haloperidol either as monotherapy or as adjunctive treatment (Jennifer M Rendell et al., 2006; Small, Klapper, Milstein,

Marhenke, & Small, 1996). However, a meta-analysis of seven randomized clinical trials (n=2037) found haloperidol shows
faster improvement in mania than risperidone, olanzapine, ziprasidone, quetiapine, and aripiprazole (Goikolea et al., 2012).

There is limited data comparing risperidone with other treatments for prevention of mania or depressive episodes in bipolar
disorder (J M Rendell & Geddes, 2006), and optimal treatment is a combination of evidence based therapy and individualized
treatment regimens (Gitlin & Frye, 2012). There is support for risperidone's superior efficacy in preventing mania compared to
aripiprazole, ziprasidone, olanzapine, lithium, quetiapine and lamotrigine (Popovic et al., 2011). Depot risperidone has been
reported as effective maintenance treatment in bipolar disorder with effect noted predominantly for preventing mania (Gigante,
Lafer, & Yatham, 2012).

In a multi-site randomized clinical trial of mania in children ages 6 through 15 years old, risperidone was found to be more
effective than lithium or divalproex, but the magnitude of the effect was affected by presence of attention deficit hyperactivity
disorder (ADHD) and study site related characteristics (Vitiello et al., 2012). These findings of superior efficacy of risperidone
compared to divalproex (Pavuluri et al., 2010) and lithium or divalproex were supported by other randomized controlled trials
(Geller et al., 2012). A review of antipsychotic use in children and young adults found second-generation antipsychotics
improved clinical global impressions in Bipolar Disorder. There was not a significant difference in efficacy between individual
atypical antipsychotics (Seida et al., 2012). This finding is supported in other studies (Gentile, 2011).

Comparison with Placebo:
In comparison to placebo, two trials found risperidone monotherapy to be significantly more efficacious in reducing manic
symptoms, leading to response, remission and sustained remission. In five trials, risperidone both as monotherapy and as
adjunctive treatment was found to have significantly lower incidence of failure to completing treatment when compared to
placebo (Jennifer M Rendell et al., 2006).

Irritability and Aggression in Autism:
There is limited data comparing risperidone with other medications for irritability and aggression in autism. A Cochrane review
of risperidone in autism (Jesner, Aref-Adib, & Coren, 2007) identified three relatively small, randomized controlled trials
showing some evidence of risperidone efficacy in irritability, repetition, and social withdrawal.

A meta-analysis of 22 studies including 6 placebo-controlled and 16 open-label studies found significant evidence for
effectiveness of risperidone in improvement of behavioral symptoms in children with autistic spectrum disorder (Sharma &
Shaw, 2012). Risperidone has the most evidence for efficacy, followed by aripiprazole in irritability of autism (Elbe & Lalani,
2012).

In a Cochrane review of atypical antipsychotics for disruptive behavior disorders in children and youths (Loy, Merry, Hetrick, &
Stasiak, 2012), authors conducted meta-analyses that showed improvement in the irritability subscale of the Aberrant Behavior
Checklist (ABC) with risperidone (n=225). There was also some improvement with risperidone in conduct problems as
measured by the Conners' Parent Rating Scale-Conduct Problem Subscale (CPRS- CP).

A review of antipsychotic use in children and young adults found second-generation antipsychotics improved clinical global impressions and behavior symptoms in disruptive behavior disorders. But, there was not a significant difference in efficacy between individual atypical antipsychotics (Seida et al., 2012). Lithium and risperidone have similar efficacy in treating disruptive behavior disorders (Ipser & Stein, 2007).

Other indications:
A meta-analysis of double-blind, randomized, placebo-controlled trials found one-third of serotonin reuptake inhibitor-resistant obsessive compulsive disorder (OCD) patients benefitted from an augmentation with antipsychotics. Authors concluded that based on a favorable risk-benefit ratio, risperidone is preferable to quetiapine and olanzapine (Dold, Aigner, Lanzenberger, & Kasper, 2012).

There is some data on antipsychotic medications in tic disorders and Tourette syndrome. Risperidone has the best evidence level for atypical antipsychotics and is considered first-line treatment for tics with aripiprazole as the second choice (Bruggeman et al., 2001; Roessner et al., 2012).

A randomized trial found no significant difference in anti-depressive properties between risperidone, quetiapine, olanzapine and ziprasidone in patients acutely admitted with psychosis (Kjelby, Jorgensen, Kroken, Loberg, & Johnsen, 2011). A Cochrane review on second-generation antipsychotics for major depressive disorder and dysthymia included 28 RCTs (n=8487) comparing amisulpride, aripiprazole, olanzapine, risperidone and quetiapine. Quetiapine was found to be more effective than placebo. Risperidone and olanzapine showed efficacy when used for treatment augmentation (Komossa, Depping, Gaudchau, Kissling, & Leucht, 2010).

A double-blind RCT showed no statistically significant difference between citalopram and risperidone in the treatment psychotic symptoms or agitation in patients with dementia (Pollock et al., 2007). Risperidone showed efficacy superior to placebo in dementia-associated agitation and psychosis (Katz et al., 1999).

A Cochrane review of antipsychotic medications for delirium found risperidone, olanzapine and low-dose haloperidol have similar efficacy in decreasing the degree and duration of delirium (Lonergan, Britton, Luxenberg, & Wyller, 2007). Another systematic review found similar efficacy in delirium improvement between risperidone, quetiapine, haloperidol, chlorpromazine and olanzapine (Seitz, Gill, & van Zyl, 2007).

There is very little evidence for the efficacy of risperidone in substance addiction. A Cochrane review on antipsychotic medications for cocaine dependence found risperidone to be superior to placebo in lowering the number of dropouts (Amato, Minozzi, Pani, & Davoli, 2007). A 14-week double-blind study comparing risperidone to olanzapine in reducing marijuana and cocaine craving as well as use found no significant improvement with either medication. There was also no statistically significant difference in effect between olanzapine and risperidone (Akerele & Levin, 2007).

10.3. Summary of Available Estimates of Comparative Effectiveness of Risperidone

In the treatment of psychosis, risperidone is more efficacious in improving positive and negative symptoms than haloperidol. It shows lower attrition rates as well as better relapse prevention compared to haloperidol. Risperidone also yields better improvement in neurocognitive domains than haloperidol.

In comparisons of risperidone with other atypical antipsychotics for treatment of psychosis, all second-generation antipsychotic medications appear to have similar efficacy though some studies show slight superiority with clozapine and olanzapine.

Risperidone is effective in reducing symptoms of mania both as monotherapy and as adjunctive

treatment. Compared to other
atypical antipsychotics in treating mania, risperidone has better efficacy and tolerability data making it a more desirable choice

within this medication group for the treatment of mania. There is some evidence that risperidone may also be superior to lithium
and divalproex in the management of acute mania.

In irritability and behavioral disturbance associated with autism, evidence supports the relative efficacy of risperidone. Among
atypical antipsychotic medications, risperidone has the most evidence for efficacy, followed by aripiprazole, in irritability of
autism

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11. Summary of Comparative Evidence on Safety of Risperidone

A systematic review was conducted using PubMed and Cochrane databases (last search September 2012). These catalogues
were searched for articles using keywords “risperidone” and “comparison” for PubMed and “risperidone” only for the Cochrane
database search. Further data was obtained through cross-referencing and a hand search of relevant literature. There were no
specifications on language.

A total of 541 abstracts in PubMed and 49 reviews in Cochrane databases were identified initially. Among these, 125 were
relevant to comparative evidence on safety for risperidone. Of the 125 relevant articles, 53 were excluded due to poor study
design, small sample size, type of article (e.g. letter to the editor), and/or Incomplete or non-available data. As a result 72 studies
and review articles were included in this summary.

Estimate of Total Patient Exposure to Date
Risperidone was first approved by the United States Food and Drug Administration in 1993 (FDA, 2012). There is no available
data estimating the total patient exposure of risperidone worldwide to date. A 2008 naturalistic study of 27 countries in 4
continents (N=3222) found that, second to olanzapine, risperidone is the most commonly prescribed atypical antipsychotic
(Dossenbach et. al., 2008). In the United States, risperidone also continues to be one of the most commonly prescribed atypical
antipsychotic medications. In 2008, there were 12.02 million U.S. prescriptions for risperidone (Alexander et. al., 2011).

Common Adverse Effects
(Micromedex 2.0, 2012)
Common side effects include edema, rash, hyperprolactinemia, weight gain, altered lipid or glucose metabolism, abdominal pain,
constipation, diarrhea, extra-pyramidal symptoms (including Parkinsonism), sedation, akathisia, tremor, cough, and fatigue.

Serious side effects include sudden cardiac death, cerebrovascular events, seizure, neuroleptic malignant syndrome, and effects
of bone marrow suppression such as leukopenia, neutropenia, and thrombocytopenia.

Psychosis
Comparison with typical antipsychotic medications
In a Cochrane review comparing risperidone versus typical antipsychotic medications (Hunter, Joy, Kennedy, Gilbody, & Song,
2003), ten randomized control trials (n=2702) found that risperidone resulted in significantly fewer general movement disorders

including extrapyramidal side effects compared to typical antipsychotic medications. Eleven RCTs (n=2524) showed that
significantly fewer persons on Risperidone used antiparkinsonian medications compared to those on typical antipsychotics.

Four randomized control trials (n=1708) found risperidone was associated with more weight gain than conventional
antipsychotics. It was also associated with higher likelihood of rhinitis than typical antipsychotics (3 RCTs, n=656).
Risperidone was found to have similar sexual side effect burden as typical antipsychotics in 2 RCTs (N=106). (Hunter et al.,
2003).

In one study risperidone treatment was associated with adverse effects on eye movement activity whereby there was a decreased
peak velocity and accuracy of saccadic eye movements compared to haloperidol treatment (Sweeney et al., 1997).

A population based cohort study of 75,445 elderly (age >65) new users of antipsychotic medications showed haloperidol to be
associated with increased risk of mortality compared to risperidone. Lowest risk was with quetiapine use. (K F Huybrechts et al.,
2012) Another study found similar associations with mortality risk, with haloperidol having the greatest risk and loxapine the
lowest (Schneeweiss, Setoguchi, Brookhart, Dormuth, & Wang, 2007). This risk trend was also seen in patients with dementia
(Kales et al., 2012).

Comparison with other atypical antipsychotic medications
In a Cochrane review that included 45 blinded randomized control trials (n=7760) comparing risperidone versus other atypical
antipsychotics (Komossa et al., 2011), risperidone was found to produce somewhat more extrapyramidal side effects than other
atypical antipsychotics. It was associated with higher use of antiparkinsonian medications compared to olanzapine (13 RCTs, n
= 2599), clozapine (6 RCTs, n=304), Ziprasidone (2RCTs, n=822) and quetiapine (6 RCTs, n = 1715). One randomized control
trial showed more Parkinsonism with risperidone compared to sertindole (n=321). In the trials reviewed, risperidone was
associated with increased prolactin levels (Komossa et al., 2011) and menstrual irregularities (McEvoy et al., 2007) compared to

other atypical antipsychotics.

Risperidone was reported to cause less weight gain than clozapine (3RCTs, n = 373), olanzapine (13 RCTs, n = 2116), and sertindole (2 RCTs, n =328), and less cholesterol elevation than quetiapine (5 RCTs, n=1433). Risperidone caused more weight gain than amisulpride (3 RCTs, n=585), and it had more cholesterol increase than aripiprazole (1 RCT, n=83) and ziprasidone (2 RCTs, n=767). Other smaller trials and reviews reflected similar results on the level of weight gain among different atypical antipsychotic medications (Bushe, Slooff, Haddad, & Karagianis, 2012; Hasnain, W Victor, & Hollett, 2012; Klemp et al., 2011; Moisan, Grégoire, Gaudet, & Cooper, 2005; Newcomer, 2005, 2007; Patel et al., 2009; Robinson et al., 2006; Sikich et al., 2008; Wood et al., 2012). This was also seen in a study focusing on non-Euro-American Societies (Bou Khalil, 2012), in Latin American populations (Brunner et al., 2006), and a Swiss psychiatric population (Choong et al., 2012). A head to head, multi-national comparison found risperidone and sertindole showed similar levels of weight gain (De Hert, Mittoux, He, & Peuskens, 2010). There is a greater risk of diabetes with olanzapine than with risperidone (Ramaswamy, Masand, & Nasrallah, 2006). This risk was found to be dose dependent in olanzapine, risperidone, and quetiapine. Aripiprazole and ziprasidone were not associated with an increased risk of diabetes (Ulcickas Yood et al., 2011).

Studies reviewed showed risperidone causes fewer seizures than clozapine (2 RCTs, n=354), prolongs QTc interval less than sertindole (2RCTs, n =495), causes less sexual dysfunction in men than in sertindole (2RCTs, n=437) and may also be less sedating than clozapine and quetiapine (Komossa et al., 2011). Clozapine is associated with significantly higher rate of nocturnal enuresis compared to risperidone, olanzapine and quetiapine (Harrison-Woolrych, Skegg, Ashton, Herbison, & Skegg, 2011).

In a Cochrane review comparing risperidone versus olanzapine for schizophrenia (Jayaram & Hosalli, 2005), participants on either medication experienced some extrapyramidal symptoms (2 RCTs, n=419). Olanzapine was associated with more weight gain, which was significant and quick in onset (2RCTs, n =984). Those on olanzapine were more likely to leave the study due to weight gain or metabolic side effects (1 RCT, n = 667). Risperidone was associated with abnormal ejaculation (2 RCTs, n = 370) and relatively more frequent insomnia. In a more recent study, the level of insomnia in risperidone long-acting injectable was found to be similar to that experienced with paliperidone palmitate (Fleischhacker et al., 2011). A meta-analysis found that patients treated with risperidone have a slightly higher rate of anticholinergic drug use than patients on olanzapine (Sauriol et al., 2001)

In a double-blind randomized controlled multicenter trial, suicidal ideation was significantly associated with clinician observed akathisia in first-episode schizophrenia. The study showed increased akathisia with haloperidol compared to risperidone but there was no significant difference with respect to suicidal ideation (Seemüller et al., 2012)

In children treated with atypical antipsychotics, short-term metabolic effects and extrapyramidal symptoms were found to be frequent. Risperidone resulted in less weight gain than olanzapine and clozapine but more than quetiapine and aripiprazole. Risperidone was also associated with more hyperprolactinemia than other atypical psychotic agents. Unlike olanzapine and quetiapine, risperidone showed no increase in triglyceride and cholesterol levels (Cohen, Bonnot, Bodeau, Consoli, & Laurent, 2012). These side effect profiles of antipsychotics in children and young adults have been replicated in other studies as well (Ben Amor, 2012; Maayan & Correll, 2011; Pringsheim, Lam, Ching, & Patten, 2011; Seida et al., 2012).

In the elderly population, atypical antipsychotic medications showed little variation in their comparative safety profiles in

nursing home residents (Krista F Huybrechts et al., 2012). A study of risk of falls and fractures in community-dwelling older
persons also found no significant difference between atypical antipsychotics (Chatterjee, Chen, Johnson, & Aparasu, 2012).

Comparison with Placebo
In a Cochrane review comparing risperidone versus placebo (Rattehalli, Jayaram, & Smith, 2010), 5 randomized control trials
(n=723) showed approximately 24% of all participants receiving either placebo or risperidone developed extrapyramidal effects.
Participants on the risperidone arm gained more weight in 2 RCTs (n=303) and had elevated prolactin compared to placebo in 2
RCTs (n =323). 1 study reported 3 participants on risperidone had prolonged QTc (n=198).

In a double-blind comparison between risperidone, quetiapine and placebo, risperidone was associated with more weight gain,
parkinsonism, akathisia and plasma prolactin changes when compared to placebo (Potkin et al., 2006)

Bipolar Disorder
A Cochrane review of Risperidone in acute mania (Rendell, Gijsman, Bauer, Goodwin, & Geddes, 2006) identified 6 trials
(n=1343) on risperidone as monotherapy or in combination with lithium, or an anticonvulsant. There is limited and somewhat
conflicting data on comparison of risperidone's safety with other medications for bipolar mania. A double blind randomized
controlled trial found risperidone and haloperidol to have comparable extrapyramidal side effects (Segal, Berk, & Brook, 1998),
while other studies show risperidone causes less extrapyramidal symptoms and sedation but more weight gain than haloperidol
(Rendell et al., 2006). Risperidone and olanzapine have been associated with higher risk of hospitalization than quetiapine. In
rapid cyclers, risperidone was associated with a higher risk of hospitalization than olanzapine (Gianfrancesco, Rajagopalan,
Goldberg, & Wang, 2007).

Irritability and Aggression in Autism
There is sparse literature comparing the safety of risperidone with other medications for irritability and aggression in autism. A
Cochrane review of risperidone in autism (Jesner, Aref-Adib, & Coren, 2007) with three relatively small, randomized controlled
trials showed weight gain as the most notable side effect associated with risperidone.

In a Cochrane review of atypical antipsychotics for disruptive behavior disorders in children and youths (Loy, Merry, Hetrick, &
Stasiak, 2012), a meta-analysis of two studies (n = 138) showed an average weight gain of 2.37 kilograms more with risperidone
than with placebo.

Summary of comparative safety of risperidone against comparators:
Risperidone is associated with less adverse side effects than haloperidol and appears to have better tolerability.

In comparison to other atypical antipsychotics, risperidone is associated with significant increase in prolactin. It is also
associated with marginally more extrapyramidal side effects.

Due to the limitations on the quantity and quality of available data, it is unclear if risperidone's other side effects are significantly
different from those of other atypical antipsychotic medications. One of the most frequent adverse effects with risperidone is
weight gain. Weight gain in risperidone is less than in clozapine, olanzapine and sertindole, but more than amisulpride.

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12. Summary of Available Data on Comparative Cost and Cost-Effectiveness of Risperidone within its Pharmacological Class/Therapeutic Group

12.1 Range of Costs

All cost information was obtained from the International Drug Price Indicator Guide1

	Package	Package Price	Unit Price
Source			
	100 Tab-cap (Tablets)	$ 3.91	0.0391/tab-cap

MEDEOR/TZ

Buyer Prices

Source	Package	Package Price	Unit Price
SAFRICA	30 Tab-cap (Tablets)	$ 1.19	0.0397 /tab-cap
OECS/PPS	20 Tab-cap (Tablets)	$ 1.24	0.0620 /tab-cap
BDS	20 Tab-cap (Tablet)	$ 1.35	0.0674 /tab-cap
CRSS	100 Tab-cap (Tablets)	$ 16.01	0.1601 /tab-cap

Median Price 0.0647/tab-cap Lowest Price 0.0397/tab-cap

High/Low Ratio 4.03 Highest Price 0.1601/tab-cap

Supplier Information
MEDEOR/TZ: Action Medeor International Healthcare, Tanzania
SAFRICA: South Africa Department of Health
OECS/PPS: Organisation of Eastern Caribbean States Pharmaceutical Procurement Service
BDS: Barbados Drug Service
CRSS: Caja Costarricense de Seguro Social, Costa Rica

1 http://erc.msh.org/dmpguide/index.cfm?search_cat=yes&display=yes&module=dmp

12.2 Comparative Cost-Effectiveness

A systematic review of the cost-effectiveness literature on risperidone was conducted (last search October 2012). A PubMed search using the keywords “risperidone cost effectiveness” yielded 165 articles. Of these, 40 were deemed relevant based on the criteria that they expressed cost-effectiveness as a range of cost per routine outcome. Three of the relevant articles were excluded based on small sample size and/or poor study design. A search of the Cochrane Database of Systematic Reviews using the same keywords yielded no additional relevant articles.

The studies are sorted into three categories: those focusing on risperidone for the treatment of schizophrenia, schizoaffective disorder, or psychosis; those focusing on bipolar disorder; and those focusing on risperidone long-acting injection (RLAI). The overall evidence suggests that risperidone can be recommended from a cost-effectiveness standpoint, as it is at worst cost-neutral compared to other atypical antipsychotic medications as well as typical antipsychotics.

Schizophrenia, Schizoaffective Disorder, Psychosis
Twenty-eight studies examined the cost-effectiveness of risperidone for the treatment of schizophrenia, schizoaffective disorder, or psychosis. Of these, four reviews of the literature were identified, three that were multi-country studies and one based in the U.S. The review papers did not provide a firm conclusion as to the cost-effectiveness of risperidone compared with olanzapine or with typical antipsychotics. One review of pharmacoeconomic studies on olanzapine for the treatment of schizophrenia in the U.S., the U.K., Spain, the Netherlands, and Germany concluded that while the data suggests that olanzapine is more cost-effective than risperidone, additional studies are required to confirm this (Foster & Goa, 1999). However, a similar study by the same authors that centered on risperidone concluded that despite high acquisition costs, risperidone may reduce the overall treatment costs of schizophrenia compared to standard treatment regimens by reducing hospitalization (Foster & Goa, 1998).
Another review of the literature on risperidone compared to conventional antipsychotics concluded that risperidone provided

improved clinical as well as quality of life outcomes in a manner that was either cost-neutral or at best cost-saving. The U.S.-based review, which identified 17 relevant articles written between 1975 and 2002, noted that while studies based on trial settings have tended to find risperidone more costly than haloperidol, those based on cohort designs and decision models have generally found it to be less costly (Basu, 2004). Taken together, published reviews of the literature on the comparative cost-effectiveness of risperidone suggest at the very least that there is insufficient evidence to conclude that risperidone lacks cost-effectiveness relative to olanzapine or to atypical antipsychotics.

A large multi-country retrospective chart review was more conclusive on comparative cost than on comparative effectiveness. The Risperidone Olanzapine Drug Outcomes studies in Schizophrenia (RODOS) program reported health economic data comparing risperidone and olanzapine for patients with diagnoses of schizophrenia or schizoaffective disorder (n=1901) across 61 inpatient treatment centers in Australia, Austria, Denmark, Great Britain, Germany, the Netherlands, Norway, Spain, and Sweden. Together with a companion paper that reported efficacy data, the study concluded that risperidone was significantly less costly (U.S. $159.9 compared to $297.5) and possibly more effective based on physician ratings (Barbui, Lintas, & Percudani, 2005) (Kasper, Jones, & Duchesne, 2001).

The vast majority of studies in this section were conducted in countries with a very high Human Development Index (HDI) based on the 2011 United Nations Development Programme Human Development Report (United Nations Development Programme, 2011): two in Australia, two in Belgium, two in Canada, one in the Czech Republic, one in France, one in Greece, three in Spain, one in Slovenia, one in Sweden, two in the U.K., and five in the U.S.

A review of cost-effectiveness from the perspective of the Australian health sector across a range interventions for schizophrenia concluded that switching patients currently on olanzapine to risperidone would result in AUD $27 million in cost saving. However, the report found that risperidone would be the most cost-effective option only for patients who experience moderate to severe side effects on typical antipsychotics-- for patients without such side effects the author recommended low-dose typicals. Replacing typical antipsychotics with risperidone had a cost per DALY of AUD 20,000 among the patient population with troublesome side-effects and AUD 48,000 overall (Vos et al., 2005) (Magnus, Carr, Mihalopoulos, Carter, & Vos, 2005). A 2-year decision-analytic model based on guidelines issued by the Australian Pharmaceutical Benefits Advisory Committee concluded that risperidone dominated haloperidol in terms of cost per favorable outcome, defined as the patient being in a response phase at the end of the 2-year period. Risperidone had a total cost of $15,549.00 and a probability of 78.9% of producing a favorable outcome compared to $18,332.00 and 58.9% for haloperidol, respectively (Alison Davies et al., 1998). While these figures may be somewhat outdated, more recent pharmacoeconomic evaluations were absent from the literature.

In an observational, non-randomized cost-effectiveness study of schizoppublhrenic patients in Belgium (n=265), no statistically significant differences were observed between risperidone and olanzapine upon net-benefit regression. Total 2-year costs were nearly identical, and health outcomes, measured using the EQ-5D index of health-related quality of life, were numerically better for risperidone but statistically indistinguishable (De Ridder & De Graeve, 2009). A 1-year semi-Markov model studying the treatment of schizophrenia in the Belgian healthcare system found that risperidone, at a cost of $36,125 and an effectiveness rate of 69.4%, dominated both olanzapine ($36,574/69.4%) and haloperidol ($36,262/67.3%). Effectiveness was measured based on a modified version of TWiST (time without symptoms and toxicity) as the average time over a 1-year period spent in a health state defined as “response with no-side effects” or “response with bearable side effects” (Lecomte et al., 2000).

According to a semi-Markov model using data from the Clinical Antipsychotic Trials for Intervention Effectiveness Study in Canada, risperidone was both less costly over a 5-year period and more effective in terms of QALYs than quetiapine and olanzapine ($21,831/3,025 compared to $26,233/3,022 and $28,563/2,982, respectively). Risperidone was less effective but less costly than ziprasidone, which had an incremental cost of $218,060 per QALY gained (McIntyre et al., 2010). A 1-year population-based study in Quebec comparing schizophrenic patients prescribed olanzapine with those prescribed olanzapine found that among patients who had not been hospitalized for mental illness prior to treatment, risperidone was both less costly and more effective in preventing hospitalization. Among patients with prior hospitalization, olanzapine was more effective but also more costly, with an ICER of CA$86,918 per year of additional effective treatment (Cooper, Moisan, Abdous, & Grégoire, 2008).

An open intent-to-treat study in the Czech Republic compared charts of schizophrenic patients treated with risperidone (n=67) to those treated with classical neuroleptics (n=67) and concluded that risperidone was significantly more expensive without leading to statistically distinguishable outcomes (Hosák & Bahbouh, 2002).

A 5-year Markov model from the perspective of the French National Health Insurance found that zuclopenthixol had a 55% effectiveness rate, as measured by time without relapse, compared to 43% for risperidone, while realizing cost savings of €1100 per patient (Hansen, François, Toumi, & Lançon, 2002).

A decision analytic model tailored to the Greek healthcare system found that palperidone extended release may result in a greater number of stable days at a lower cost than risperidone (272.5 days at €7,030 compared to 265.5 days at €7,082). However, risperidone was cheaper and more effective than quetiapine (260.7 / €8,321), ziprasidone (260.5/€7,713), and aripiprazole (258.6 / €7,807) (Geitona et al., 2008).

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A decision analytic model for reducing schizophrenia relapses in Spain found that risperidone dominated haloperidol at an ICER of €4,353/QALY compared to €4,593/QALY (García-Ruiz et al., 2012). A 12-month Markov model from the perspective of third party payers in Spain found that risperidone was dominated by ziprasidone in terms of cost per time with psychotic symptoms controlled and without adverse reactions. Among a cohort of 1000 patients, ziprasidone had 9610 effective months at a cost of €9,444,512 compared to 9503 months/€10,339,961 for risperidone. According to the authors, few other studies have investigated cost per clinical event prevented among drugs for schizophrenia (Bobes, Cañas, Rejas, & Mackell, 2004).

A population-level comparison of different clinical interventions for reducing the burden of schizophrenia in Spain found that typical antipsychotics alone cost $45, 833 per DALY averted whereas generic risperidone cost a somewhat less $45, 022 per DALY averted. Addition of psychosocial treatment and case management to either typical antipsychotics or generic risperidone significantly enhanced cost effectiveness according this measure. Combining typical antipsychotics with psychosocial treatment/case management cost U.S. $25,069 per DALY averted, and combining generic risperidone with psychosocial treatment/case management led to the most cost effective clinical intervention at $24, 672 cost per DALY averted (Gutierrez-Recacha, Chisholm, Haro, Salvador-Carulla, & Ayuso-Mateos, 2006).

A decision analytic model comparing amisulpride, aripiprazole, haloperidol (oral formulation), haloperidol (depot formulation), olanzapine, quetiapine, risperidone (oral formulation), risperidone (depot formulation) and ziprasidone for the treatment of outpatient chronic schizophrenia from the perspective of the Slovenian healthcare payer

concluded that risperidone and olanzapine were the most cost-effective in terms of keeping patients in remission (Obradovic, Mrhar, & Kos, 2007).

In a Markov model study examining 5-year treatment strategy options in Sweden, risperidone and other atypical antipsychotics were found to be more cost-effective as well as clinically superior to haloperidol; each atypical had a cost per QALY of approximately 490,000 Swedish kroner compared to 500,140 for haloperidol. However, risperidone was slightly dominated by sertindole (Lindström, Eberhard, Fors, Hansen, & Sapin, 2011).

A Markov model comparing the cost-effectiveness of aripiprazole, olanzapine, quetiapine, and risperidone in the UK for treating stable schizophrenic patients found that risperidone was second to aripiprazole in terms of cost per QALYs gained (Andrew Davies et al., 2008). A retrospective chart review of patients in the U.K. with schizophrenia or schizoaffective disorder (n=501) concluded that risperidone had both a shorter mean time to effectiveness and a lower cost than olanzapine. While incidence of adverse effects was similar, patients on risperidone had an average of 9 fewer days in the hospital (Taylor, Wright, & Libretto, 2003).

Based on the projections of a 1-year Monte Carlo Micro-Simulation model in the U.S., olanzapine Oral Disintegrating Tablet (Total Cost $9808, Mean QALYs 0.747) dominated Risperidone ODT and was cost-effective compared with Risperidone standard oral tablets (ICER > $30,000) (Ascher-Svanum et al., 2012). However, risperidone and risperidone ODT dominated aripiprazole and aripiprazole ODT, respectively, at costs/mean QALYs of $8881/0.718 compared to $12,598/0.715 and $10,922/0.731 compared to $12,863/0.728. A separate U.S. micro-simulation model study also found oral olanzapine to be dominant over oral risperidone in terms of cost per QALY (Furiak et al., 2009). In contrast, a decision analysis model evaluating the cost-effectiveness of atypical antipsychotics for treating schizophrenia based on the Positive and Negative Symptom Scale found that risperidone dominated both olanzapine and haloperidol. For 16 weeks of treatment, risperidone had a cost of $13,409 per patient and a clinical efficacy of 63%, compared to $13,591.57/60% for olanzapine and $15,513.38/34% for haloperidol (Bounthavong & Okamoto, 2007). A multi-attribute utility theory study analysis analyzing efficacy in terms of 1-year relapse prevention, adverse effects, cost, and adherence, (assigned weights of 35%, 35%, 20%, and 10%, respectively), found that risperidone was neither the most dominated nor the most dominant. Specifically, aripiprazole had the highest utility score at 75.8, followed by ziprasidone (71.8), risperidone (69.0), quetiapine, and olanzapine (65.9) (Bettinger, Shuler, Jones, & Wilson, 2007).

A comparison of risperidone and olanzapine for the treatment of psychosis in the elderly at an inpatient center in Virginia found that the cost of risperidone was one-third that of olanzapine, while treatment outcomes, assessed using the Positive and Negative Syndrome Scale for Schizophrenia, the Cohen-Mansfield Agitation Inventory, and length of hospitalization, were statistically indistinguishable (Verma, Orengo, Kunik, Hale, & Molinari, 2001).

Overall, the evidence in very high HDI countries suggests that risperidone is at least cost-neutral relative to both typical antipsychotics and to other atypicals. Given the comparable efficacy of olanzapine to risperidone, data comparing the cost-effectiveness of these two drugs are of particular importance. Few articles found olanzapine to be dominant over risperidone, and thus it is safe to conclude that risperidone is at least cost-neutral relative to its closest competitor on efficacy.

Two studies were based in countries with a high HDI: one in Brazil and one in Mexico. A 5-year Markov model using data from a municipality in Southern Brazil found that risperidone as well as haloperidol were more cost-effective than olanzapine, with

cost/utility ratios in U.S. dollars per QALY at 1414.90 and 944.89 compared to 2470.57 (Lindner, Marasciulo, Farias, & Grohs, 2009). In Mexico, a 5-year decision analytic Markov model determined that olanzapine was comparable in terms of cost to risperidone and was slightly more effective in terms of preventing relapse and clinical outcome scores on the Brief Psychiatric Rating Scale (Palmer, Brunner, Ruíz-flores, Paez-agraz, & Revicki, 2002). While it is important to be cautious in drawing conclusions from only two studies, these findings suggest that the risperidone may not be as well established as a cost-effective drug in less developed countries.

Bipolar Disorder

Three papers on the cost-effectiveness of risperidone for the treatment of bipolar disorder were identified, all in very high HDI countries.

A discrete event simulation model based on four randomized controlled trials conducted in the Netherlands found that the combination of lithium and risperidone was less costly than that of lithium and quetiapine for the management of acute mania in bipolar I disorder (monotherapy options were more costly than combination therapy). Over an 84 day time horizon, lithium/risperidone cost €2,365 per patient compared to €2,555 for lithium/quetiapine. Meanwhile, switching from lithium/risperidone to the lower side-effect combination of lithium/quetiapine is predicted to prevent 1530 serious side effects but at an additional cost of €1,900,000 per 10,000 patients (Klok et al., 2007).

In the treatment of bipolar disorder with atypical antipsychotics in the U.S., one study found that risperidone was associated with statistically indistinguishable overall health care costs and effectiveness in terms of preventing hospitalization to aripiprazole. In addition, risperidone had statistically significantly lower pharmacy costs than aripiprazole (Kim, You, Pikalov, Van-Tran, & Jing, 2011). In contrast, a randomized open-label trial in the U.S. comparing 1-year cost-effectiveness of initial treatment with olanzapine (n=229) to risperidone (n=229) found that the two were equivalent in terms of cost, with higher antipsychotic costs for olanzapine offset by the resulting reduction in costs for additional services such as hospitalization. Olanzapine was found to have significantly higher social effectiveness than risperidone based on the Lehman Quality of Life Scale (Tunis et al., 2006).

The relative paucity of studies on bipolar disorder necessitates caution in interpreting the findings. At the very least, the available data do not suggest that risperidone is less cost-effective compared to other interventions.

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Risperidone Long-Acting Injection

In the literature on RLAI, two studies were conducted in very high HDI countries, one in Spain and one in the U.S. One study was also conducted in Taiwan, which is not listed separately in the 2011 Human Development Report.

A 24-month observational study of schizophrenic patients enrolled in the international electronic Schizophrenia Treatment Adherence database concluded that switching to RLAI from previous antipsychotic treatment was cost-effective because it prevented relapsing and hospitalization (Olivares, Rodriguez-Martinez, Burón, Alonso-Escolano, & Rodriguez-Morales, 2008).

A 1-year mirror image analysis using the Taiwanese national claim-based database found that while RLAI was associated with reduction of service uses in schizophrenia treatment, this was offset by the rise in medication and outpatient costs (Chang, Tang, Huang, McCrone, & Su, 2012).

A one-year micro-simulation economic decision model in the U.S. found that olanzapine LAI dominated RLAI, at costs/QALYs of $14,063/0.711 compared to $15,207/0.667 (Furiak et al., 2011).

One study was conducted in a country with a medium HDI. RLAI was found to be more cost-effective than quetiapine and olanzapine for long-term maintenance treatment of schizophrenia in China based on a decision analytical model that calculated costs per successfully treated patient. Successful treatment was defined as responding to initial treatment and neither requiring a change in treatment nor having more than two episodes of clinical deterioration over a 2-year time period (Yang et al., 2009).
Two multi-country reviews of the literature were also identified. A review of cost-effectiveness studies on risperidone long-acting injection (1999-2011) concluded that “overall cost—effectiveness in a wide array of different healthcare systems and diverse patient populations has been demonstrated with RLAI” (P. Chue & Chue, 2012). A separate review of cost-effectiveness studies concluded that RLAI has demonstrated overall effectiveness in keeping medical costs down and reducing healthcare resource utilization as well as hospitalization rates (Keith, 2009).

Among the studies reviewed in the first paper, a discrete event simulation model studying the treatment of schizophrenia from the perspective of the German healthcare system found that over a 5-year time period, long-acting risperidone avoided 0.22 and 0.33 relapses per patient while realizing cost savings of €2017 and €6096 per patient compared with haloperidol depot and olanzapine, respectively. A discrete event model for Canada found that over a 5-year time period, long-acting risperidone saved Can$6908 and Can$13,130 while avoiding 0.28 and 0.54 relapses per patient compared with haloperidol depot and oral risperidone, respectively in the treatment of high-risk, non-compliant patients with schizophrenia (P. S. Chue, Heeg, Buskens, & van Hout, 2005). However, not all studies showed a clear benefit. One randomized trial of U.S. Veterans Health Administration patients with unstable schizoaffective disorder or schizophrenia (n=369) concluded that RLAI raised medication costs without improving outcomes or lowering hospital or health care costs (Barnett, Scott, Krystal, & Rosenheck, 2012).

According the review papers identified, the comparative cost-effectiveness literature favors of RLAI.

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13. Summary of the Regulatory Status of Risperidone

Risperidone was originally developed by Janssen Pharmaceuticals and approved for use in schizophrenia by the United States Food and Drug Administration (FDA) on Dec 29, 1993 (FDA, 2012). In 2003, it received FDA approval for the short-term treatment of acute manic or mixed episodes associated with Bipolar I Disorder in adults; in 2006, for the treatment of irritability with autism in children and adolescents 5 to 16 years old. A year later, risperidone became the first atypical antipsychotic medication to gain FDA approval for the short-term treament of manic or mixed episodes of Bipolar I disorder in children and adolescents aged 10 to 17, as well as for the treatment of schizophrenia in adolescents aged 13 to 17 (FDA, 2007). Risperidone became available as a generic medication in 2008 (FDA, 2012).

Risperidone, originally developed by Janssen-Cilag, is registered with the European Medicines Agency and is approved for use in all 27 member states of the European Union (European Medicines Agency, 2012). The indications for use are similar to those in the U.S. including schizophrenia and moderate to severe manic episodes of mania in bipolar disorder (European Medicines Agency, 2008).

In 2003, Janssen Pharmaceutica Inc issued a “Dear Healthcare Professional” letter in the United States stating changes to the prescribing information for risperidone. It added information regarding cerebrovascular adverse events in elderly patients with dementia-related psychosis (FDA, 2004). In 2005, the FDA issued an alert for increased mortality in patients with dementia-related psychosis treated with atypical antipsychotics, including risperidone. At the current time, similar to other atypical antipsychotic medications, risperidone carries a "black box warning" for dementia-related psychosis (FDA, 2005).

The long-acting injection form, Risperdal Consta, received FDA approval for treatment of schizophrenia in 2003 (FDA, 2012). It is also registered in many countries around the world including the European Union, Australia, New Zealand, Switzerland, Brazil, South Africa, Korea and the Philippines among others (Australian Government Department of Health and Ageing, 2010).

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U.S. Food and Drug Administration (FDA). Risperdal (risperidone) dear healthcare professional letter. Aug 2004.
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Last accessed: Oct 6, 2012.

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14. Availability of Pharmacoepial Standards for Risperidone

British Pharmacopoeia: Yes
European Pharmacopoeia: Yes
Indian Pharmacopoeia: No
International Pharmacopoeia: No
United States Pharmacopoeia: Yes

References

British Pharmacopoeia: http://www.pharmacopoeia.co.uk/
Last accessed Oct 7, 2012.

European Pharmacopoeia 7th Edition: http://www.edqm.eu/en/european-pharmacopoeia-publications-1401.html
Last accessed Oct 7, 2012.

Indian Pharmacopoeia: http://ipc.nic.in/
Last accessed Oct 7, 2012.

InternationalPharmacopoeia:
http://www.who.int/medicines/publications/pharmacopoeia/overview/en/index.html
Last accessed Oct 7, 2012.

United States Pharmacopoeia: http://www.usp.org/
Last accessed Oct 7, 2012.

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15. Proposed New Text for the WHO Model Formulary*

----------INDICATIONS AND USAGE----------
Risperidone is an atypical antipsychotic agent indicated for:
- Treatment of schizophrenia in adults and adolescents aged 13-17 years
- Alone, or in combination with lithium or valproate, for the short-term treatment of acute manic or mixed episodes associated with Bipolar I Disorder in adults, and alone in children and adolescents aged 10-17 years
- Treatment of irritability associated with autistic disorder in children and adolescents aged 5-16 years

	Initial Dose	Titration	Target Dose	Effective Dose
Schizophrenia/Psychosis in non-emergent settings- Adults	1mg/day in 2 divided doses	1mg daily	4-8 mg daily	4-16 mg /day
Schizophrenia- Adolescents	0.5mg/day	0.5-1mg daily	3mg/day	1-6mg/day
Bipolar Mania- Adults	2-3mg/day	1mg daily	1-6mg/day	1-6mg/day
Bipolar Mania in children/adolescents	0.5mg/day	0.5 – 1mg daily	2.5mg/day	0.5–6mg/day
Irritability associated with autistic disorder	0.25mg/day (<20kg) 0.5mg/day (≥20 kg)	0.25-0.5mg at ≥ 2 weeks	0.5 mg /day (<20 kg) 1 mg /day (≥20 kg)	0.5-3mg /day

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----------DOSAGE FORMS AND STRENGTHS----------
- Tablets 0.25 mg, 1 mg, 2 mg
- Oral Solution: 1 mg/mL – 30 mL bottle
- Risperidone long-acting depot microspheres formulation for deep intramuscular administration 25 mg vial/kit

----------CONTRAINDICATIONS----------
• Known hypersensitivity to the product

----------WARNINGS AND PRECAUTIONS----------
• Cerebrovascular events, including stroke, in elderly patients with dementia-related psychosis.
• Neuroleptic Malignant Syndrome
• Tardive dyskinesia
• Hyperglycemia and diabetes mellitus
• Hyperprolactinemia
• Orthostatic hypotension
• Leukopenia, Neutropenia, and Agranulocytosis: has been reported with antipsychotics, including risperidone. Patients with a history of a clinically significant low white blood cell count (WBC) or a drug-induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and discontinuation of risperidone should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors.
• Potential for cognitive and motor impairment
• Seizures
• Disruption of body temperature regulation
• Increased sensitivity in patients with Parkinson’s disease or those with dementia with Lewy bodies

----------ADVERSE REACTIONS----------
The most common adverse reactions in clinical trials (≥10%) were somnolence, appetite

increased, fatigue, rhinitis, upper respiratory tract infection, vomiting, coughing, urinary incontinence, saliva increased, constipation, fever, Parkinsonism, dystonia, abdominal pain, anxiety, nausea, dizziness, dry mouth, tremor, rash, akathisia, and dyspepsia.

The most common adverse reactions that were associated with discontinuation from clinical trials were somnolence, nausea, abdominal pain, dizziness, vomiting, agitation, and akathisia. effects, hypotensive effects of other drugs with this potential may be enhanced.

----------DRUG INTERACTIONS----------

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- Due to CNS effects, use caution when administering with other centrally-acting drugs. Avoid alcohol. Due to hypotensive, hypotensive effects of other drugs with this potential may be enhanced
- Effects of levodopa and dopamine agonists may be antagonized.
- Cimetidine and ranitidine increase the bioavailability of risperidone.
- Clozapine may decrease clearance of risperidone.
- Fluoxetine and paroxetine increase plasma concentrations of risperidone.
- Carbamazepine and other enzyme inducers decrease plasma concentrations of risperidone.

----------USE IN SPECIFIC POPULATIONS----------

- Nursing Mothers: should not breast feed.
- Pediatric Use: safety and effectiveness not established for schizophrenia less than 13 years of age, for bipolar mania less than 10 years of age, and for autistic disorder less than 5 years of age.
- Elderly or debilitated; severe renal or hepatic impairment; predisposition to hypotension
or for whom hypotension poses a risk: Lower initial dose (0.5 mg twice daily), followed by increases in dose in increments of no more than 0.5 mg twice daily. Increases to dosages above 1.5 mg twice daily should occur at intervals of at least 1 week. (8.5, 2.4)

*(Adapted from www.fda.gov, last accessed on 11/11/12: http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020272s056,020588s044,021346s033,021444s03lbl.pdf)

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APPENDIX
Letters of Support

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MINISTRY OF HEALTH
Third Floor, East Block Building
Belmopan, Belize, Central America.
Phone: 501-822-2325/2363 Fax: 501-822-2942/2055
seniorsecretary@health.gov.bz

REF: ADM/33/12(94)

October 1, 2012

The Secretary of the 19th Expert Committee on the Selection and Use of Essential Medicines
Medicine Access and Rational Use (MAR)
Department of Essential Medicines and Health Products (EMP)
World Health Organization
20 Avenue Appia
CH-1211 Geneva 27
Switzerland

Dear Secretariat,

I am writing to you on behalf of the Ministry of Health in Belize in support of the

application being made by Dr. Craig Katz and his colleagues at the Mount Sinai School of Medicine to have Risperidone added to the List of Essential Medications. We have collaborated with them for over six years on meeting mental health needs in our own country and see their decision to make this application on behalf of people around the world as showing great initiative and wisdom. We have much experience with Risperidone.

We believe that at least one atypical antipsychotic medication should be considered an essential part of any formulary, and our experience definitely supports that it should be Risperidone. I would like to make a special appeal that it be included in all of its formulations, including the long-acting injection.

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Respectfully,

Claudia Cayetano, M.D.
Head Psychiatrist

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Risperidone

http://bipolar-disorder.emedtv.com/risperidone/risperidone-p5.html December 09, 2014

Risperidone is a medication used to treat bipolar disorder, schizophrenia, and irritability due to autism. This eMedTV resource offers an overview of risperidone ...

People who take too much risperidone may have overdose symptoms that could include: People who take too much risperidone may have overdose symptoms that could include:

If you happen to overdose, seek medical attention immediately.

The medication should be stored at room temperature, away from moisture and heat. The medication should be stored at room temperature, away from moisture and heat. Risperidone tablets and liquid should be stored in an airtight container. Keep risperidone M-Tabs in their original foil packaging until just before use.

Keep risperidone and all other medications out of the reach of children.

What Should I Do If I Miss a Dose? If you do not take your dose as scheduled, take your missed dose as soon as you remember. If it is almost time for your next dose, skip the missed dose and continue with your regular schedule. Do not take a double dose of risperidone. If you do not take your dose as scheduled, take your missed dose as soon as you remember. If it is almost time for your next dose, skip the missed dose and continue with your regular schedule. Do not take a double dose of risperidone.

Risperidone tablets are available in the following strengths: Risperidone tablets are available in the following strengths:

Orally disintegrating risperidone M-Tabs are available in the following strengths:

Risperidone liquid comes in one strength -- risperidone Oral Solution 1 mg per mL.

Risperdal, Risperdal Consta (risperidone) dosing, indications, interactions, adverse effects, and more

http://reference.medscape.com/drug/risperdal-consta-risperidone-342986 December 09, 2014

Medscape - Schizophrenia, bipolar disorder-specific dosing for Risperdal, Risperdal Consta (risperidone), frequency-based adverse effects, comprehensive interactions ...

Medscape's clinical reference is the most authoritative and accessible point-of-care medical reference for physicians and healthcare professionals, available online and via all major mobile devices. All content is free.

The clinical information represents the expertise and practical knowledge of top physicians and pharmacists from leading academic medical centers in the United States and worldwide.

The topics provided are comprehensive and span more than 30 medical specialties, covering:

More than 6000 evidence-based and physician-reviewed disease and condition articles are organized to rapidly and comprehensively answer clinical questions and to provide in-depth information in support of diagnosis, treatment, and other clinical decision-making. Topics are richly illustrated with more than 40,000 clinical photos, videos, diagrams, and radiographic images.

More than 1000 clinical procedure articles provide clear, step-by-step instructions and include instructional videos and images to allow clinicians to master the newest techniques or to improve their skills in procedures they have performed previously.

More than 100 anatomy articles feature clinical images and diagrams of the human body's major systems and organs. The articles assist in the understanding of the anatomy involved in treating specific conditions and performing procedures. They can also facilitate physician-patient discussions.

More than 7100 monographs are provided for prescription and over-the-counter drugs, as well as for corresponding brand-name drugs, herbals, and supplements. Drug images are also included.

Our Drug Interaction Checker provides rapid access to tens of thousands of interactions between brand and generic drugs, over-the-counter drugs, and supplements. Check mild interactions to serious contraindications for up to 30 drugs, herbals, and supplements at a time.

Access health plan drug formulary information when looking up a particular drug, and save time and effort for you and your patient. Choose from our complete list of over 1800 insurance plans across all 50 US states. Customize your Medscape account with the health plans you accept, so that the information you need is saved and ready every time you look up a drug on our site or in the Medscape app. Easily compare tier status for drugs in the same class when considering an alternative drug for your patient.

Medscape Reference features 129 medical calculators covering formulas, scales, and classifications. Plus, more than 600 drug monographs in our drug reference include integrated dosing calculators.

Hundreds of image-rich slideshow presentations visually engage and challenge readers while expanding their knowledge of both common and uncommon diseases, case presentations, and current controversies in medicine.

Click on citations within drug and disease topics in our clinical reference to review the clinical evidence on MEDLINE. Plus, search the MEDLINE database for journal articles.

Medscape is the leading online destination for healthcare professionals seeking clinical information. In addition to clinical reference tools, Medscape offers:

Risperidone - What Is It, Side Effects, How to Take

http://www.lifescript.com/health/centers/alzheimers/drugs/risperidone.aspx December 09, 2014

What is risperidone? Learn about risperidone side effects, how to take risperidone and more.

[Posted 06/13/2011]ISSUE:FDA notified healthcare professionals and the public of medication error reports in which patients were given risperidone (Risperdal) instead of ropinirole (Requip) and vice versa. In some cases, patients who took the wrong medication needed to be hospitalized.

The FDA determined that the factors contributing to the confusion between the two products include:

BACKGROUND:Risperidone (Risperdal) is an antipsychotic medication used to treat mental illnesses including schizophrenia, bipolar disorder, and irritability associated with autistic disorder. Ropinirole (Requip) is a dopamine agonist used in the treatment of Parkinson’s disease and Restless Legs Syndrome.

RECOMMENDATION:Healthcare Professionals are reminded to clearly print or spell out the medication name on prescriptions and make certain their patients know the name of their prescribed medication and their reason for taking it. For more information visit the FDA website at: and .

Studies have shown that older adults with dementia (a brain disorder that affects the ability to remember, think clearly, communicate, and perform daily activities and that may cause changes in mood and personality) who take antipsychotics (medications for mental illness) such as risperidone have an increased risk of death during treatment. Older adults with dementia may also have a greater chance of having a stroke or mini-stroke during treatment. Tell your doctor and pharmacist if you are taking furosemide (Lasix).

Risperidone (DB00734)

http://www.drugbank.ca/drugs/DB00734 December 09, 2014

Identification; Name: Risperidone: Accession Number: DB00734 (APRD00187) Type: small molecule: Groups: approved, investigational: Description: Risperidone, a ...

Risperidone, a benzisoxazole derivative, is an atypical antipsychotic drug with high affinity for 5-hydrotryptamine (5-HT) and dopamine D2 receptors. It is used primarily in the management of schizophrenia, inappropriate behavior in severe dementia and manic episodes associated with bipolar I disorder. Risperidone is effective for treating the positive and negative symptoms of schizophrenia owing to its affinity for its “loose” binding affinity for dopamine D2 receptors and additional 5-HT antagonism compared to first generation antipsychotics, which are strong, non-specific dopamine D2 receptor antagonists.

Extensively metabolized by hepatic cytochrome P450 2D6 isozyme to 9-hydroxyrisperidone, which has approximately the same receptor binding affinity as risperidone. Hydroxylation is dependent on debrisoquine 4-hydroxylase and metabolism is sensitive to genetic polymorphisms in debrisoquine 4-hydroxylase. Risperidone also undergoes N-dealkylation to a lesser extent.

Side Effects of Risperdal (Risperidone) Drug Center

http://www.rxlist.com/risperdal-side-effects-drug-center.htm December 09, 2014

Find a comprehensive guide to possible side effects when taking Risperdal (Risperidone) for Professionals, Patients, and Caregivers.

The FDA package insert formatted in easy-to-find categories for health professionals and clinicians.

The following are discussed in more detail in other sections of the labeling:

The most common adverse reactions in clinical trials (> 5% and twice placebo) were parkinsonism, akathisia, dystonia, tremor, sedation, dizziness, anxiety, blurred vision, nausea, vomiting, upper abdominal pain, stomach discomfort, dyspepsia, diarrhea, salivary hypersecretion, constipation, dry mouth, increased appetite, increased weight, fatigue, rash, nasal congestion, upper respiratory tract infection, nasopharyngitis, and pharyngolaryngeal pain.

The most common adverse reactions that were associated with discontinuation from clinical trials (causing discontinuation in > 1% of adults and/or > 2% of pediatrics) were nausea, somnolence, sedation, vomiting, dizziness, and akathisia [see ADVERSE REACTIONS, Discontinuations Due to Adverse Reactions].

The data described in this section are derived from a clinical trial database consisting of 9803 adult and pediatric patients exposed to one or more doses of RISPERDAL® for the treatment of schizophrenia, bipolar mania, autistic disorder, and other psychiatric disorders in pediatrics and elderly patients with dementia. Of these 9803 patients, 2687 were patients who received RISPERDAL® while participating in double-blind, placebo-controlled trials. The conditions and duration of treatment with RISPERDAL® varied greatly and included (in overlapping categories) double-blind, fixed- and flexible-dose, placebo- or active-controlled studies and open-label phases of studies, inpatients and outpatients, and short-term (up to 12 weeks) and longer-term (up to 3 years) exposures. Safety was assessed by collecting adverse events and performing physical examinations, vital signs, body weights, laboratory analyses, and ECGs.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in

the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Table 8 lists the adverse reactions reported in 2% or more of RISPERDAL®-treated adult patients with schizophrenia in three 4- to 8-week, double-blind, placebo-controlled trials.

Table 8: Adverse Reactions in ≥ 2% of RISPERDAL®-Treated Adult Patients (and greater than placebo) with Schizophrenia in Double-Blind, Placebo-Controlled Trials

Table 9 lists the adverse reactions reported in 5% or more of RISPERDAL®-treated pediatric patients with schizophrenia in a 6-week double-blind, placebo-controlled trial.

Table 9: Adverse Reactions in ≥ 5% of RISPERDAL®-Treated Pediatric Patients (and greater than placebo) with Schizophrenia in a Double-Blind Trial

Table 10 lists the adverse reactions reported in 2% or more of RISPERDAL®-treated adult patients with bipolar mania in four 3-week, double-blind, placebo-controlled monotherapy trials.

Table 10: Adverse Reactions in ≥ 2% of RISPERDAL®-Treated Adult Patients (and greater than placebo) with Bipolar Mania in Double-Blind, Placebo-Controlled Monotherapy Trials

Table 11 lists the adverse reactions reported in 2% or more of RISPERDAL®-treated adult patients with bipolar mania in two 3-week, double-blind, placebo-controlled adjuvant therapy trials.

Table 11: Adverse Reactions in ≥ 2% of RISPERDAL®-Treated Adult Patients (and greater than placebo) with Bipolar Mania in Double-Blind, Placebo-Controlled Adjunctive Therapy Trials

Table 12 lists the adverse reactions reported in 5% or more of RISPERDAL®-treated pediatric patients with bipolar mania in a 3-week double-blind, placebo-controlled trial.

Table 12: Adverse Reactions in ≥ 5% of RISPERDAL®-Treated Pediatric Patients (and greater than placebo) with Bipolar Mania in Double-Blind, Placebo-Controlled Trials

Table 13 lists the adverse reactions reported in 5% or more of RISPERDAL®-treated pediatric patients treated for irritability associated with autistic disorder in two 8-week, double-blind, placebo-controlled trials and one 6-week double-blind, placebo-controlled study.

Table 13: Adverse Reactions in ≥ 5% of RISPERDAL®-Treated Pediatric Patients (and greater than placebo) Treated for Irritability Associated with Autistic Disorder in Double-Blind, Placebo-Controlled Trials

The following additional adverse reactions occurred across all placebo-controlled, active-controlled, and open-label studies of RISPERDAL® in adults and pediatric patients.

Nervous System Disorders: balance disorder, disturbance in attention, dysarthria, unresponsive to stimuli, depressed level of consciousness, movement disorder, transient ischemic attack, coordination abnormal, cerebrovascular accident, speech disorder, syncope, loss of consciousness, hypoesthesia, tardive dyskinesia, dyskinesia, cerebral ischemia, cerebrovascular disorder, neuroleptic malignant syndrome, diabetic coma, head titubation

The following is a list of additional adverse reactions that have been reported during the premarketing evaluation of RISPERDAL® CONSTA®, regardless of frequency of occurrence:

Approximately 7% (39/564) of RISPERDAL®-treated patients in double-blind, placebo-controlled trials discontinued treatment due to an adverse reaction, compared with 4% (10/225) who were receiving placebo. The adverse reactions associated with discontinuation in 2 or more RISPERDAL®-treated patients were:

Table 14: Adverse Reactions Associated With Discontinuation in 2 or More RISPERDAL®Treated Adult Patients in Schizophrenia Trials

Discontinuation for extrapyramidal symptoms (including Parkinsonism, akathisia, dystonia, and tardive dyskinesia) was 1% in placebo-treated patients, and 3.4% in active control-treated patients in a double-

blind, placebo- and active-controlled trial.

Approximately 7% (7/106), of RISPERDAL®-treated patients discontinued treatment due to an adverse reaction in a double-blind, placebo-controlled trial, compared with 4% (2/54) placebo-treated patients. The adverse reactions associated with discontinuation for at least one RISPERDAL®-treated patient were dizziness (2%), somnolence (1%), sedation (1%), lethargy (1%), anxiety (1%), balance disorder (1%), hypotension (1%), and palpitation (1%).

In double-blind, placebo-controlled trials with RISPERDAL® as monotherapy, approximately 6% (25/448) of RISPERDAL®-treated patients discontinued treatment due to an adverse event, compared with approximately 5% (19/424) of placebo-treated patients. The adverse reactions associated with discontinuation in RISPERDAL®-treated patients were:

Table 15: Adverse Reactions Associated With Discontinuation in 2 or More RISPERDAL®Treated Adult Patients in Bipolar Mania Clinical Trials

In a double-blind, placebo-controlled trial 12% (13/111) of RISPERDAL®-treated patients discontinued due to an adverse reaction, compared with 7% (4/58) of placebo-treated patients. The adverse reactions associated with discontinuation in more than one RISPERDAL®-treated pediatric patient were nausea (3%), somnolence (2%), sedation (2%), and vomiting (2%).

In the two 8-week, placebo-controlled trials in pediatric patients treated for irritability associated with autistic disorder (n = 156), one RISPERDAL®-treated patient discontinued due to an adverse reaction (Parkinsonism), and one placebo-treated patient discontinued due to an adverse event.

Data from two fixed-dose trials in adults with schizophrenia provided evidence of dose-relatedness for extrapyramidal symptoms associated with RISPERDAL® treatment.

Two methods were used to measure extrapyramidal symptoms (EPS) in an 8-week trial comparing 4 fixed doses of RISPERDAL® (2, 6, 10, and 16 mg/day), including (1) a Parkinsonism score (mean change from baseline) from the Extrapyramidal Symptom Rating Scale, and (2) incidence of spontaneous complaints of EPS:

Similar methods were used to measure extrapyramidal symptoms (EPS) in an 8-week trial comparing 5 fixed doses of RISPERDAL® (1, 4, 8, 12, and 16 mg/day):

Class Effect: Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue. While these symptoms can occur at low doses, they occur more frequently and with greater severity with high potency and at higher doses of first generation antipsychotic drugs. An elevated risk of acute dystonia is observed in males and younger age groups.

Adverse event data elicited by a checklist for side effects from a large study comparing 5 fixed doses of RISPERDAL® (1, 4, 8, 12, and 16 mg/day) were explored for dose-relatedness of adverse events. A Cochran-Armitage Test for trend in these data revealed a positive trend ($p < 0.05$) for the following adverse reactions: somnolence, vision abnormal, dizziness, palpitations, weight increase, erectile dysfunction, ejaculation disorder, sexual function abnormal, fatigue, and skin discoloration.

Weight gain was observed in short-term, controlled trials and longer-term uncontrolled studies in adult and pediatric patients [see WARNINGS AND PRECAUTIONS and Use in Specific Populations].

Between-group comparisons for pooled placebo-controlled trials in adults revealed no statistically significant differences between risperidone and placebo in mean changes from baseline in ECG parameters, including QT, QTc, and PR intervals, and heart rate. When all RISPERDAL® doses were pooled from randomized controlled trials in several indications, there was a mean increase in heart rate of 1 beat per minute compared to no change for placebo patients. In short-term schizophrenia trials, higher doses of risperidone (8-16 mg/day) were associated with a higher mean increase in heart rate compared to placebo (4-6 beats per minute). In pooled placebo-controlled acute mania trials in adults, there were small decreases in mean heart rate, similar among all treatment groups.

In the two placebo-controlled trials in children and adolescents with autistic disorder (aged 5 - 16 years) mean changes in heart rate were an increase of 8.4 beats per minute in the RISPERDAL® groups and

6.5 beats per minute in the placebo group. There were no other notable ECG changes.

In a placebo-controlled acute mania trial in children and adolescents (aged 10 - 17 years), there were no significant changes in ECG parameters, other than the effect of RISPERDAL® to transiently increase pulse rate (< 6 beats per minute). In two controlled schizophrenia trials in adolescents (aged 13 - 17 years), there were no clinically meaningful changes in ECG parameters including corrected QT intervals between treatment groups or within treatment groups over time.

The following adverse reactions have been identified during postapproval use of risperidone. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These adverse reactions include: alopecia, anaphylactic reaction, angioedema, atrial fibrillation, cardiopulmonary arrest, diabetic ketoacidosis in patients with impaired glucose metabolism, dysgeusia, hypoglycemia, hypothermia, ileus, inappropriate antidiuretic hormone secretion, intestinal obstruction, jaundice, mania, pancreatitis, pituitary adenoma, precocious puberty, pulmonary embolism, QT prolongation, sleep apnea syndrome, sudden death, thrombocytopenia, thrombotic thrombocytopenic purpura, urinary retention, and water intoxication.

RightDiagnosis.com

http://www.rightdiagnosis.com/medical/risperidone.htm December 09, 2014

Risperidone information including symptoms, causes, diseases, symptoms, treatments, and other medical and health issues.

Risperidone: A selective blocker of DOPAMINE D2 RECEPTORS and SEROTONIN 5-HT2 RECEPTORS that acts as an atypical antipsychotic agent. It has been shown to improve both positive and negative symptoms in the treatment of SCHIZOPHRENIA.

Source: Diseases Database

Risperidone: selective blocker of dopamine D2 and serotonin-5-HT2 receptors that acts as an atypical antipsychotic agent; has been shown to improve both positive and negative symptoms in the treatment of schizophrenia.

Source: CRISP

Risperidone: A selective blocker of DOPAMINE D2 RECEPTORS and SEROTONIN 5-HT2 RECEPTORS that acts as an atypical antipsychotic agent. It has been shown to improve both positive and negative symptoms in the treatment of SCHIZOPHRENIA.

Source: MeSH 2007

These medical condition or symptom topics may be relevant to medical information for Risperidone:

Because many drug names share similar spellings or sound almost identical when spoken, it is possible to mistake the name of a particular medication. Other drugs that are sometimes confused with Risperidone include:

Brands, Medical Use, Clinical Data

http://www.druglib.com/activeingredient/risperidone/ December 09, 2014

Risperidone is now the most commonly prescribed antipsychotic medication in the United States. Mechanism of Action. Blockade of dopaminergic D2 receptors in the ...

For the treatment of schizophrenia. Risperidone is an atypical antipsychotic medication. It is most often used to treat delusional psychosis (including schizophrenia), but risperidone is also used to treat some forms of bipolar disorder and psychotic depression. It also has shown some success in treating symptoms of Asperger's Syndrome and autism. Risperidone is now the most commonly prescribed antipsychotic medication in the United States. Blockade of dopaminergic D2 receptors in the limbic system alleviates positive symptoms of schizophrenia such as hallucinations, delusions, and erratic behavior and speech. Blockade of serotonergic 5-HT receptors in the mesocortical tract, causes an excess of dopamine and an increase in dopamine transmission, resulting in an increase in dopamine transmission and an elimination of core negative symptoms. Dopamine receptors in the nigrostriatal

pathway are not affected by risperidone and extrapyramidal effects are avoided. Like other 5-HT antagonists, risperidone also binds at alpha(1)-adrenergic receptors and, to a lesser extent, at histamine H1 and alpha(2)-adrenergic receptors. Well absorbed. The absolute oral bioavailability of risperidone is 70% (CV=25%). The relative oral bioavailability of risperidone from a tablet is 94% (CV=10%) when compared to a solution. Symptoms of overdose include drowsiness, sedation, tachycardia, hypotension, and extrapyramidal symptoms. LD =82.1mg/kg (orally in mice). RISPERDAL® (risperidone) is contraindicated in patients with a known hypersensitivity to the product. The interactions of RISPERDAL® and other drugs have not been systematically evaluated. Given the primary CNS effects of risperidone, caution should be used when RISPERDAL® is taken in combination with other centrally acting drugs and alcohol. Because of its potential for inducing hypotension, RISPERDAL® may enhance the hypotensive effects of other therapeutic agents with this potential. RISPERDAL® may antagonize the effects of levodopa and dopamine agonists. Amytriptyline does not affect the pharmacokinetics of risperidone or the active antipsychotic fraction. Cimetidine and ranitidine increased the bioavailability of risperidone, but only marginally increased the plasma concentration of the active antipsychotic fraction. Chronic administration of clozapine with risperidone may decrease the clearance of risperidone. In a drug interaction study in schizophrenic patients, 11 subjects received risperidone titrated to 6 mg/day for 3 weeks, followed by concurrent administration of carbamazepine for an additional 3 weeks. During co-administration, the plasma concentrations of risperidone and its pharmacologically active metabolite, 9-hydroxyrisperidone, were decreased by about 50%. Plasma concentrations of carbamazepine did not appear to be affected. The dose of risperidone may need to be titrated accordingly for patients receiving carbamazepine, particularly during initiation or discontinuation of carbamazepine therapy. Co-administration of other known enzyme inducers (e.g., phenytoin, rifampin, and phenobarbital) with risperidone may cause similar decreases in the combined plasma concentrations of risperidone and 9-hydroxyrisperidone, which could lead to decreased efficacy of risperidone treatment. Fluoxetine (20 mg QD) and paroxetine (20 mg QD) have been shown to increase the plasma concentration of risperidone 2.5-2.8 fold and 3-9 fold respectively. Fluoxetine did not affect the plasma concentration of 9-hydroxyrisperidone. Paroxetine lowered the concentration of 9-hydroxyrisperidone an average of 13%. When either concomitant fluoxetine or paroxetine is initiated or discontinued, the physician should re-evaluate the dosing of RISPERDAL®. The effects of discontinuation of concomitant fluoxetine or paroxetine therapy on the pharmacokinetics of risperidone and 9-hydroxyrisperidone have not been studied. Repeated oral doses of risperidone (3 mg BID) did not affect the exposure (AUC) or peak plasma concentrations (C) of lithium (n=13). Valproate Repeated oral doses of risperidone (4 mg QD) did not affect the pre-dose or average plasma concentrations and exposure (AUC) of valproate (1000 mg/day in three divided doses) compared to placebo (n=21). However, there was a 20% increase in valproate peak plasma concentration (C) after concomitant administration of risperidone. RISPERDAL® (0.25 mg BID) did not show a clinically relevant effect on the pharmacokinetics of digoxin. Drugs That Inhibit CYP 2D6 and Other CYPIsozymes Risperidone is metabolized to 9-hydroxyrisperidone by CYP 2D6, an enzyme that is polymorphic in the population and that can be inhibited by a variety of psychotropic and other drugs. Drug interactions that reduce the metabolism of risperidone to 9-hydroxyrisperidone would increase the plasma concentrations of risperidone and lower the concentrations of 9-hydroxyrisperidone. Analysis of clinical studies involving a modest number of poor metabolizers (n 70) does not suggest that poor and extensive metabolizers have different rates of adverse effects. No comparison of effectiveness in the two groups has been made. In vitro studies showed that drugs metabolized by other CYPisozymes, including 1A1, 1A2, 2C9, 2C19, and 3A4, are only weak inhibitors of risperidone metabolism. There were no significant interactions between risperidone and erythromycin. In vitro studies indicate that risperidone is a relatively weak inhibitor of CYP 2D6. Therefore, RISPERDAL® is not expected to substantially inhibit the clearance of drugs that are metabolized by this enzymatic pathway. In drug interaction studies, risperidone did not significantly affect the pharmacokinetics of donepezil and galantamine, which are metabolized by CYP 2D6.

The official site for risperidone information

http://www.risperidone.com/ December 09, 2014

What is Risperidone? Risperidone is an atypical antipsychotic medication. It is most often used to treat delusional psychosis (including schizophrenia).

Risperidone is an atypical antipsychotic medication. It is most often used to treat delusional psychosis (including schizophrenia).

This medication is also used to treat some forms of bipolar disorder and psychotic depression.

Risperidone works by changing the effects of chemicals in the brain. Some of the brand names of

risperidone is the US are Belivon®, Rispen®, Risperdal®.

Risperidone?

https://uk.answers.yahoo.com/question/index?qid=20080722111615AAKedNQ December 09, 2014

Risperidone is an atypical antipsychotic, and is actually a relatively new drug. It is quite sedative and has 'calming' effects i.e. reduces anxiety ...

I'm 15 years old and have been depressed for a long time now. I've only told people in the last three months and since then I've seen a few doctors. There were recently two incidents which I ended up in hospital afterwards. The first was when I went out with my friends and got so drunk I got alcohol poisoning. I used to drink to give myself confidence and then stayed sober for months, so my tolerance for alcohol went down. I haven't drank since and won't, it's not an addicted thing. The second was when I took an overdose of 7 paracetamol, 8 co-codamol and 15 aspirin before school. When I got to school I couldn't breathe or keep my eyes open properly and was pale and shaky. On both occasions, I saw a psychiatrist on the ward who reviewed me and then discharged me.

I saw her again today and she has put me on medication starting straight away. I am on Risperidone and also something else which will calm me down and help me sleep, also stop me being so implusive but I can't remember the

Question.com

https://www.question.com/medication/risperidone.html December 09, 2014

Generic Name: risperidone (oral) (ris PER i done) Brand Names: Risperdal, Risperdal M-Tab. What is the most important information I should know about risperidone?

Risperidone is not for use in psychotic conditions related to dementia. Risperidone may cause heart failure, sudden death, or pneumonia in older adults with dementia-related conditions.

Do not give this medication to a child without a doctor's advice.

While you are taking risperidone, you may be more sensitive to temperature extremes such as very hot or cold conditions. Avoid getting too cold, or becoming overheated or dehydrated. Drink plenty of fluids, especially in hot weather and during exercise. It is easier to become dangerously overheated and dehydrated while you are taking risperidone.

Risperidone can cause side effects that may impair your thinking or reactions. Be careful if you drive or do anything that requires you to be awake and alert.

Avoid drinking alcohol. It can increase some of the side effects of risperidone.

Stop using risperidone and call your doctor at once if you have fever, stiff muscles, confusion, sweating, fast or uneven heartbeats, restless muscle movements in your face or neck, tremor (uncontrolled shaking), trouble swallowing, feeling light-headed, or fainting.

There may be other drugs not listed that can affect risperidone. Tell your doctor about all the prescription and over-the-counter medications you use. This includes vitamins, minerals, herbal products, and drugs prescribed by other doctors. Do not start using a new medication without telling your doctor.

Risperidone is an antipsychotic medication. It works by changing the effects of chemicals in the brain.

Risperidone is used to treat schizophrenia and symptoms of bipolar disorder (manic depression). Risperidone is also used in autistic children to treat symptoms of irritability.

Risperidone may also be used for purposes other than those listed in this medication guide.

Risperidone is not for use in psychotic conditions related to dementia. Risperidone may cause heart failure, sudden death, or pneumonia in older adults with dementia-related conditions.

You should not use this medication if you are allergic to risperidone.

If you have any of these other conditions, you may need a dose adjustment or special tests to safely take this medication:

Risperidone may cause you to have high blood sugar (hyperglycemia). Talk to your doctor if you have any signs of hyperglycemia such as increased thirst or urination, excessive hunger, or weakness. If you are diabetic, check your blood sugar levels on a regular basis while you are taking risperidone.

The risperidone orally disintegrating tablet may contain phenylalanine. Talk to your doctor before using this form of risperidone if you have phenylketonuria (PKU).

FDA pregnancy category C. It is not known whether risperidone is harmful to an unborn baby. Before taking this medication, tell your doctor if you are pregnant or plan to become pregnant during treatment.

It is not known whether risperidone passes into breast milk or if it could harm a nursing baby. Do not use this medication without telling your doctor if you are breast-feeding a baby.

Do not give this medication to a child without a doctor's advice.

Take this medication exactly as it was prescribed for you. Do not take the medication in larger amounts, or take it for longer than recommended by your doctor. Follow the directions on your prescription label.

Risperidone can be taken with or without food.

It is important to take risperidone regularly to get the most benefit. Get your prescription refilled before you run out of medicine completely.

Measure the liquid form of risperidone with a special dose-measuring spoon or cup, not a regular table spoon. If you do not have a dose-measuring device, ask your pharmacist for one.

Do not mix the liquid form of risperidone with cola or tea.

It may take several weeks of using this medicine before your symptoms improve. For best results, keep using the medication as directed. Talk with your doctor if your symptoms do not improve.

Store risperidone at room temperature away from moisture, light, and heat. Do not allow the liquid form of risperidone to freeze.

Take the missed dose as soon as you remember. If it is almost time for your next dose, skip the missed dose and take the medicine at the next regularly scheduled time. Do not take extra medicine to make up the missed dose.

Seek emergency medical treatment if you think you have used too much of this medicine.

Overdose symptoms may include drowsiness, fast heart rate, feeling light-headed, fainting, and restless muscle movements in your eyes, tongue, jaw, or neck.

While you are taking risperidone, you may be more sensitive to temperature extremes such as very hot or cold conditions. Avoid getting too cold, or becoming overheated or dehydrated. Drink plenty of fluids, especially in hot weather and during exercise. It is easier to become dangerously overheated and dehydrated while you are taking risperidone.

Risperidone can cause side effects that may impair your thinking or reactions. Be careful if you drive or do anything that requires you to be awake and alert.

Avoid drinking alcohol. It can increase some of the side effects of risperidone.

Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

Stop using risperidone and call your doctor at once if you have any of these serious side effects:

Less serious side effects may include:

This is not a complete list of side effects and others may occur. Call your doctor for medical advice

about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Before you take risperidone, tell your doctor if you regularly use other medicines that make you sleepy (such as cold or allergy medicine, narcotic pain medicine, sleeping pills, muscle relaxers, and medicine for seizures, depression, or anxiety). They can add to sleepiness caused by risperidone.

Also tell your doctor if you are taking any of the following medicines:

This list is not complete and there may be other drugs that can interact with risperidone. Tell your doctor about all the prescription and over-the-counter medications you use. This includes vitamins, minerals, herbal products, and drugs prescribed by other doctors. Do not start using a new medication without telling your doctor.

Your pharmacist can provide more information about risperidone.

Remember, keep this and all other medicines out of the reach of children, never share your medicines with others, and use this medication only for the indication prescribed.

Every effort has been made to ensure that the information provided by Cerner Multum, Inc. ('Multum') is accurate, up-to-date, and complete, but no guarantee is made to that effect. Drug information contained herein may be time sensitive. Multum information has been compiled for use by healthcare practitioners and consumers in the United States and therefore Multum does not warrant that uses outside of the United States are appropriate, unless specifically indicated otherwise. Multum's drug information does not endorse drugs, diagnose patients or recommend therapy. Multum's drug information is an informational resource designed to assist licensed healthcare practitioners in caring for their patients and/or to serve consumers viewing this service as a supplement to, and not a substitute for, the expertise, skill, knowledge and judgment of healthcare practitioners. The absence of a warning for a given drug or drug combination in no way should be construed to indicate that the drug or drug combination is safe, effective or appropriate for any given patient. Multum does not assume any responsibility for any aspect of healthcare administered with the aid of information Multum provides. The information contained herein is not intended to cover all possible uses, directions, precautions, warnings, drug interactions, allergic reactions, or adverse effects. If you have questions about the drugs you are taking, check with your doctor, nurse or pharmacist.

Risperidone

http://www.medschat.com/Drugs/Risperidone/ December 09, 2014

Welcome to the Risperidone information hub. Featuring active ingredients, dosages, related medications, and Risperidone forums.

sizodon plus side effects reaction after stopping

my son is taking sizodon plus for over 2 years he has a govt job and he intends to stop this medicine is it advisable to do so please advise ## Hi, Humnum! If he's been taking it for that long, then stopping it suddenly isn't advisable. Sizodon contains the active ingredient Risperidone, which is an atypical antipsychotic that's used to treat various mental health issues. However, a sudden withdrawal of it could cause serious rebound effects, that may result in mental health disturbances and major depression. Learn more Sizodon details here. Thus, if he wishes to stop taking it, he should consult his doctor and slowly taper the medication under their supervision. Is there anything else I can help with? ## I am using sizodonplus from past two year because of some chemical cha...

my son is taking sizodon plus for over 2 years he has a govt job and he intends to stop this medicine is it advisable to do so please advise ## Hi, Humnum! If he's been taking it for that long, then stopping it suddenly isn't advisable. Sizodon contains the active ingredient Risperidone, which is an atypical antipsychotic that's used to treat various mental health issues. However, a sudden withdrawal of it could cause serious rebound effects, that may result in mental health disturbances and major depression. Learn more Sizodon details here. Thus, if he wishes to stop taking it, he should consult his doctor and slowly taper the medication under their supervision. Is there anything else I can help with? ## I am using sizodonplus from past two year because of some chemical cha...

risperidone 6 mg

I was on risperidone from 2002 to 2003 then quit because my dad doesn't believe I'm mental health. I

have now started it again in 2011 to present. I am currently on 6 MG and have not had a period for over a year. Has anyone experienced this? I haven't been ovulating either. I want to have another baby and was wondering if I'll start ovulating again. I would quit taking it while pregnant but can't get pregnant while on it. Will it ever go away? Will I ever have another baby? Any advice and experience stories would be great. ## Have you discussed your concerns with your doctor? There may be other medications you can take that will allow you to cycle normally to get pregnant. Many of these antipsychotics can throw off the female menstrual cycle, but it usually returns t...

I was on risperidone from 2002 to 2003 then quit because my dad doesn't believe I'm mental health. I have now started it again in 2011 to present. I am currently on 6 MG and have not had a period for over a year. Has anyone experienced this? I haven't been ovulating either. I want to have another baby and was wondering if I'll start ovulating again. I would quit taking it while pregnant but can't get pregnant while on it. Will it ever go away? Will I ever have another baby? Any advice and experience stories would be great. ## Have you discussed your concerns with your doctor? There may be other medications you can take that will allow you to cycle normally to get pregnant. Many of these antipsychotics can throw off the female menstrual cycle, but it usually returns t...

pill m r 12

Who is Mr bars ## Hi Russel, How's it going? I'm not sure who "Mr. Bars" is supposed to be or if that was an accidental typo? But looking at the pill imprint of "M R12", this fits the description of a 2mg Risperidone tablet, used for treating schizophrenia and bipolar disorder. If you want to look it up for verification, the manufacturer is reported to be Mylan, and the pill itself carries a National Drug Code of 00378-3512. I hope this helps! Please feel free to post back if you have any other details to add to your post.

Who is Mr bars ## Hi Russel, How's it going? I'm not sure who "Mr. Bars" is supposed to be or if that was an accidental typo? But looking at the pill imprint of "M R12", this fits the description of a 2mg Risperidone tablet, used for treating schizophrenia and bipolar disorder. If you want to look it up for verification, the manufacturer is reported to be Mylan, and the pill itself carries a National Drug Code of 00378-3512. I hope this helps! Please feel free to post back if you have any other details to add to your post.

Sizodon 1mg

Let me know the side effects and as well as good effects if I use this Pill as suggested my Doctor himself. ## Sizodon is listed as containing the active ingredient Risperidone, which is an atypical antipsychotic that's used to treat various mental health conditions. Side effects may include nausea, dizziness, dry mouth, sedation and weight gain. Learn more Sizodon details here. Why has your doctor recommended it? ## hi, my husband take the medicine sizidon 3mg more than 5 years. but in few days he take sizidon 1mg. is it safe I am worried about him.please advice

Let me know the side effects and as well as good effects if I use this Pill as suggested my Doctor himself. ## Sizodon is listed as containing the active ingredient Risperidone, which is an atypical antipsychotic that's used to treat various mental health conditions. Side effects may include nausea, dizziness, dry mouth, sedation and weight gain. Learn more Sizodon details here. Why has your doctor recommended it? ## hi, my husband take the medicine sizidon 3mg more than 5 years. but in few days he take sizidon 1mg. is it safe I am worried about him.please advice

risperidone 3mg

What are the common side effects for a women with Bipolar Disorder on 3mg Risperidone. ## Hello, Olivia! How are you? The most common side effects associated with this medication include nausea, dizziness, somnolence, fatigue and weight changes. 3mgs is a pretty high dose, so I'd expect the somnolence and fatigue to be pretty pronounced on that dosage. Is there anything else I can help with?

What are the common side effects for a women with Bipolar Disorder on 3mg Risperidone. ## Hello, Olivia! How are you? The most common side effects associated with this medication include nausea, dizziness, somnolence, fatigue and weight changes. 3mgs is a pretty high dose, so I'd expect the somnolence and fatigue to be pretty pronounced on that dosage. Is there anything else I can help with?

r 1 on one side and prtron other

It's a oval pill and it is off white in color and small r 1 on one side and Prtron on the other. ## The tablet with the R 1 on one side and PATR on the other contains 1mg of Risperidone, which is a very potent antipsychotic. Side effects may include nausea, dizziness, drowsiness, weight gain, sedation and somnolence. Is there anything else I can help with?

It's a oval pill and it is off white in color and small r 1 on one side and Prtron on the other. ## The tablet with the R 1 on one side and PATR on the other contains 1mg of Risperidone, which is a very potent antipsychotic. Side effects may include nausea, dizziness, drowsiness, weight gain, sedation and somnolence. Is there anything else I can help with?

small white pill m on one side and an r the other

I have a small white pill with m on one side and a r on the other side ## Hello, Jeff! How are you? This tablet contains 0.25mgs of Risperidone, which is a very potent antipsychotic that's most commonly used to treat psychiatric disorders. Side effects may include nausea, dizziness, drowsiness, somnolence, sedation and weight changes. Is there anything else I can help with?

I have a small white pill with m on one side and a r on the other side ## Hello, Jeff! How are you? This tablet contains 0.25mgs of Risperidone, which is a very potent antipsychotic that's most commonly used to treat psychiatric disorders. Side effects may include nausea, dizziness, drowsiness, somnolence, sedation and weight changes. Is there anything else I can help with?

peach round zc76

What med is it? It has nothing on the opposite side.. About as big around as a watch battery....small. ## Hello, Vicki! How are you? This tablet contains 2mgs of Risperidone, which is a very potent antipsychotic. Side effects may include nausea, dizziness, weight gain and somnolence. Is there anything else I can help with?

What med is it? It has nothing on the opposite side.. About as big around as a watch battery....small. ## Hello, Vicki! How are you? This tablet contains 2mgs of Risperidone, which is a very potent antipsychotic. Side effects may include nausea, dizziness, weight gain and somnolence. Is there anything else I can help with?

respiradone and novelon can be used together

Can respiradone and novelon tablets can used together. I am not getting periods bec of 1mg respiradone tablet so doctor prescribed novelon tablets. Can it be used together. ## Dear Hema, does your Dr know u r on Risperidone? If he's the one who gave u both medications, then u have nothing 2 worry about. Besides, your pharmacy would catch this, if there were a problem.

Can respiradone and novelon tablets can used together. I am not getting periods bec of 1mg respiradone tablet so doctor prescribed novelon tablets. Can it be used together. ## Dear Hema, does your Dr know u r on Risperidone? If he's the one who gave u both medications, then u have nothing 2 worry about. Besides, your pharmacy would catch this, if there were a problem.

Risperidone..serta-100...parkin

Risperidone..serta-100...parkin These are the medicines used by my friend aged 28 . He used to say that these are to reduce work pressure.He use this on daily basis . For what are these for.

Risperidone..serta-100...parkin These are the medicines used by my friend aged 28 . He used to say that these are to reduce work pressure.He use this on daily basis . For what are these for.

Risperidone (/rsprdon/ ri-SPAIR-i-dohn) (trade name Risperdal, and generics) is an antipsychotic drug mainly used to treat schizophrenia (including adolescent schizophrenia), schizoaffective disorder, the mixed and manic states of bipolar disorder, and irritability in people with autism. Risperidone is a second-generation atypical antipsychotic.[2] It is a dopamine antagonist possessing anti-serotonergic, anti-adrenergic and anti-histaminergic properties. Adverse effects of risperidone includ...

RISPERIDONE- risperidone tablet

http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=5EADDA0E-FAF8-4B3C-851E-DA5A5A127242 December 09, 2014

These highlights do not include all the information needed to use Risperidone Tablets, Oral Solution, and Orally Disintegrating Tablets safely and effectively.

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. In two of four placebo-controlled trials in elderly patients with dementia-related psychosis, a higher incidence of mortality was observed in patients treated with furosemide plus risperidone when compared to patients treated with risperidone alone or with placebo plus furosemide. No pathological mechanism has been identified to explain this finding, and no consistent pattern for cause of death was observed. Risperidone is not approved for the treatment of dementia-related psychosis [see Boxed Warning].

Antipsychotic drugs including risperidone can cause a potentially fatal symptom complex referred to as Neuroleptic Malignant Syndrome (NMS). Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered mental status, and autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase (CPK), myoglobinuria, rhabdomyolysis, and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases in which the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology. The management of NMS should include: (1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; (2) intensive symptomatic treatment and medical monitoring; and (3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, prescribe risperidone in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that: (1) is known to respond to antipsychotic drugs, and (2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient treated with risperidone, consider drug discontinuation. However, some patients may require treatment with risperidone despite the presence of the syndrome.

Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include hyperglycemia, dyslipidemia, and body weight gain. While all of the drugs in the class have been shown to produce some metabolic changes, each drug has its own specific risk profile. Hyperglycemia and diabetes mellitus, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, have been reported in patients treated with atypical antipsychotics including risperidone. Assessment of the relationship

between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics, including risperidone, should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics, including risperidone, should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics, including risperidone, should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics, including risperidone, should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic, including risperidone, was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of risperidone. Pooled data from three double-blind, placebo-controlled schizophrenia studies and four double-blind, placebo-controlled bipolar monotherapy studies are presented in Table 2. Table 2. Change in Random Glucose from Seven Placebo-Controlled, 3- to 8-Week, Fixed- or Flexible-Dose Studies in Adult Subjects with Schizophrenia or Bipolar Mania In longer-term, controlled and uncontrolled studies, risperidone was associated with a mean change in glucose of +2.8 mg/dL at Week 24 (n=151) and +4.1 mg/dL at Week 48 (n=50). Data from the placebo-controlled 3- to 6-week study in children and adolescents with schizophrenia (13–17 years of age), bipolar mania (10–17 years of age), or autistic disorder (5 to 17 years of age) are presented in Table 3. Table 3. Change in Fasting Glucose from Three Placebo-Controlled, 3- to 6-Week, Fixed-Dose Studies in Children and Adolescents with Schizophrenia (13–17 years of age), Bipolar Mania (10–17 years of age), or Autistic Disorder (5 to 17 years of age) In longer-term, uncontrolled, open-label extension pediatric studies, risperidone was associated with a mean change in fasting glucose of +5.2 mg/dL at Week 24 (n=119). Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics. Pooled data from 7 placebo-controlled, 3- to 8- week, fixed- or flexible-dose studies in adult subjects with schizophrenia or bipolar mania are presented in Table 4. Table 4. Change in Random Lipids from Seven Placebo-Controlled, 3- to 8-Week, Fixed- or Flexible-Dose Studies in Adult Subjects with Schizophrenia or Bipolar Mania In longer-term, controlled and uncontrolled studies, risperidone was associated with a mean change in (a) non-fasting cholesterol of +4.4 mg/dL at Week 24 (n=231) and +5.5 mg/dL at Week 48 (n=86); and (b) non-fasting triglycerides of +19.9 mg/dL at Week 24 (n=52). Pooled data from 3 placebo-controlled, 3- to 6-week, fixed-dose studies in children and adolescents with schizophrenia (13–17 years of age), bipolar mania (10–17 years of age), or autistic disorder (5–17 years of age) are presented in Table 5. Table 5. Change in Fasting Lipids from Three Placebo-Controlled, 3- to 6-Week, Fixed-Dose Studies in Children and Adolescents with Schizophrenia (13–17 Years of Age), Bipolar Mania (10–17 Years of Age), or Autistic Disorder (5 to 17 Years of Age) In longer-term, uncontrolled, open-label extension pediatric studies, risperidone was associated with a mean change in (a) fasting cholesterol of +2.1 mg/dL at Week 24 (n=114); (b) fasting LDL of -0.2 mg/dL at Week 24 (n=103); (c) fasting HDL of +0.4 mg/dL at Week 24 (n=103); and (d) fasting triglycerides of +6.8 mg/dL at Week 24 (n=120). Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended. Data on mean changes in body weight and the proportion of subjects meeting a weight gain criterion of 7% or greater of body weight from 7 placebo-controlled, 3- to 8- week, fixed- or flexible-dose studies in adult subjects with schizophrenia or bipolar mania are presented in Table 6. Table 6. Mean Change in Body Weight (kg) and the Proportion of Subjects with ≥7% Gain in Body Weight From Seven Placebo-Controlled, 3- to 8-Week, Fixed- or Flexible-Dose Studies in Adult Subjects With Schizophrenia or Bipolar Mania In longer-term, controlled and uncontrolled studies, risperidone was associated with a mean change in weight of +4.3 kg at Week 24 (n=395) and +5.3 kg at Week 48 (n=203). Data on mean changes in body weight and the proportion of subjects meeting the criterion of ≥7% gain in body weight from nine placebo-controlled, 3- to 8-week, fixed-dose studies in children and adolescents with schizophrenia (13–17 years of age), bipolar mania (10–17 years of age), autistic disorder (5–17 years of age), or other psychiatric disorders (5–17 years of age) are presented in Table 7. Table 7. Mean Change in Body Weight (kg) and the Proportion of Subjects With ≥7% Gain in Body Weight From Nine Placebo-Controlled, 3- to 8-Week, Fixed-Dose Studies in Children and Adolescents With Schizophrenia (13–17 Years of Age), Bipolar Mania (10–17 Years of Age), Autistic Disorder (5 to 17 Years of Age) or Other Psychiatric Disorders (5–17 Years of Age) In longer-term, uncontrolled, open-label extension pediatric studies, risperidone was associated with a mean change in weight of +5.5 kg at

Week 24 (n=748) and +8.0 kg at Week 48 (n=242). In a long-term, open-label extension study in adolescent patients with schizophrenia, weight increase was reported as a treatment-emergent adverse event in 14% of patients. In 103 adolescent patients with schizophrenia, a mean increase of 9.0 kg was observed after 8 months of risperidone treatment. The majority of that increase was observed within the first 6 months. The average percentiles at baseline and 8 months, respectively, were 56 and 72 for weight, 55 and 58 for height, and 51 and 71 for body mass index. In long-term, open-label trials (studies in patients with autistic disorder or other psychiatric disorders), a mean increase of 7.5 kg after 12 months of risperidone treatment was observed, which was higher than the expected normal weight gain (approximately 3 to 3.5 kg per year adjusted for age, based on Centers for Disease Control and Prevention normative data). The majority of that increase occurred within the first 6 months of exposure to risperidone. The average percentiles at baseline and 12 months, respectively, were 49 and 60 for weight, 48 and 53 for height, and 50 and 62 for body mass index. In one 3-week, placebo-controlled trial in children and adolescent patients with acute manic or mixed episodes of bipolar I disorder, increases in body weight were higher in the risperidone groups than the placebo group, but not dose related (1.90 kg in the risperidone 0.5–2.5 mg group, 1.44 kg in the risperidone 3–6 mg group, and 0.65 kg in the placebo group). A similar trend was observed in the mean change from baseline in body mass index. When treating pediatric patients with risperidone for any indication, weight gain should be assessed against that expected with normal growth.

As with other drugs that antagonize dopamine D2 receptors, risperidone elevates prolactin levels and the elevation persists during chronic administration. Risperidone is associated with higher levels of prolactin elevation than other antipsychotic agents. Hyperprolactinemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotropin secretion. This, in turn, may inhibit reproductive function by impairing gonadal steroidogenesis in both female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds. Long-standing hyperprolactinemia when associated with hypogonadism may lead to decreased bone density in both female and male subjects. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in a patient with previously detected breast cancer. An increase in pituitary gland, mammary gland, and pancreatic islet cell neoplasia (mammary adenocarcinomas, pituitary and pancreatic adenomas) was observed in the risperidone carcinogenicity studies conducted in mice and rats [see Nonclinical Toxicology (13.1)]. Neither clinical studies nor epidemiologic studies conducted to date have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is considered too limited to be conclusive at this time.

Risperidone may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period, probably reflecting its alpha-adrenergic antagonistic properties. Syncope was reported in 0.2% (6/2607) of risperidone-treated patients in Phase 2 and 3 studies in adults with schizophrenia. The risk of orthostatic hypotension and syncope may be minimized by limiting the initial dose to 2 mg total (either once daily or 1 mg twice daily) in normal adults and 0.5 mg twice daily in the elderly and patients with renal or hepatic impairment [see Dosage and Administration (2.1, 2.4)]. Monitoring of orthostatic vital signs should be considered in patients for whom this is of concern. A dose reduction should be considered if hypotension occurs. Risperidone should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, and conditions which would predispose patients to hypotension, e.g., dehydration and hypovolemia. Clinically significant hypotension has been observed with concomitant use of risperidone and antihypertensive medication.

Class Effect: In clinical trial and/or postmarketing experience, events of leukopenia/neutropenia have been reported temporally related to antipsychotic agents, including risperidone. Agranulocytosis has also been reported. Possible risk factors for leukopenia/neutropenia include pre-existing low white blood cell count (WBC) and history of drug-induced leukopenia/neutropenia. Patients with a history of a clinically significant low WBC or a drug-induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and discontinuation of risperidone should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors. Patients with clinically significant neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count <1000/mm3) should discontinue risperidone and have their WBC followed until recovery.

Somnolence was a commonly reported adverse reaction associated with risperidone treatment, especially when ascertained by direct questioning of patients. This adverse reaction is dose-related, and in a study utilizing a checklist to detect adverse events, 41% of the high-dose patients (risperidone 16 mg/day) reported somnolence compared to 16% of placebo patients. Direct questioning is more sensitive for detecting adverse events than spontaneous reporting, by which 8% of risperidone 16 mg/day patients and 1% of placebo patients reported somnolence as an adverse reaction. Since risperidone has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that risperidone therapy does not affect them adversely.

Risperidone

http://www.herbs2000.com/medica/risperidone.htm December 09, 2014

Brand names of risperidone. Risperdal; The FDA approved (December 1993) risperidone is mainly used to treat schizophrenia, bipolar mania and autism, as it is an ...

The FDA approved (December 1993) risperidone is mainly used to treat schizophrenia, bipolar mania and autism, as it is an atypical antipsychotic drug. The difference between atypical antipsychotic drugs and typical antipsychotic drugs is that the former lowers extra-pyramidal (nerves that coordinate movement) side effects and constipation. The injectable form of the medication, which is a long acting form, is known as Risperdal Consta. Things you need to tell your physician before taking risperidone Communicate to the doctor if you are allergic to risperidone or any other medicine before you begin taking the medication. Also inform him if you are taking or plan to take any other prescribed or non-prescribed remedies like vitamins, herbal products or nutritional supplements. The doctor should also know if you have a history of drug abuse like overusing prescribed medication or if you have used street drugs and consumed alcohol in large amounts. Also inform the doctor if you have had any of these medical conditions like Parkinson's disease, swallowing difficulties, breast cancer, irregular heart beats, angina, heart failure, heart attack, stroke, high or low blood pressure, seizures, any other heart disease, liver and kidney disease and also if anyone in your family is or has been afflicted with diabetes. In case you have ever had to stop taking medication for mental illness because of severe side effects then let your doctor know this as well. The doctor must be told if you are pregnant or plan on becoming pregnant, and also he should be informed if you do become pregnant while you are taking risperidone. Rule out breast feeding while you are on the drug. If you are slated for a surgery, including dental intervention, then the surgeon or dentist need to be told that you are taking risperidone. Risperidone can make some people drowsy so till you know how it affects you do not drive a vehicle or operate machinery. Alcohol could also add to the feeling of drowsiness and so it is best to avoid it while on the medication. Even if you do not have diabetes you could be inflicted with hyperglycemia (an increase in blood sugar levels) if you are taking risperidone. Communicate to the doctor immediately if after taking risperidone you have had symptoms like extreme thirst, extreme hunger, frequent urination, weakness and blurred vision. These symptoms are an indication of high blood sugar and if it is left untreated then it could lead to a more serious and life threatening condition called ketoacidosis. Symptoms of ketoacidosis are dry mouth, upset stomach, short breath, fruity smelling breath and lowered consciousness. Ketoacidosis needs to be treated in the early stages or it could be fatal. Risperidone makes it difficult to heat up the body once it is cold and also it is difficult to cool down if the temperature of the body has increased due to vigorous physical activity. You must tell the doctor, before you take risperidone, if you are likely to be exposed to either extremely high or low temperature. Other side effects seen while using risperidone are dizziness, light-headedness and fainting when you get up from a lying position and are especially noticeable when you first start taking the medication. The best way to prevent these symptoms is to get out of bed slowly, resting your feet on the floor first before standing up fully. Phenylketonuria is a condition which requires a special diet in order to prevent mental illness. So if you have this condition be cautious as the risperidone tablet that disintegrates orally, contains phenylalanine. Risperidone is used to treat psychotic conditions like schizophrenia which are characterized by symptoms where distorted thoughts, emotions and perceptions are common and lead to mental disorders. The medication is also used in symptoms of severe dementia like behavioural disturbances. How to use risperidone Take the medication exactly as prescribed with or without food. Initially the doctor may give you a small dose and increase it slowly as your body gets used to the medication. The dosage is based on factors like your medical condition and how you respond to the medication. So even if you are feeling better or mentally alert continue with the medication as directed. In case you have been prescribed the liquid form of the medicine then use the special measuring device and not a household spoon as the dose measured out could be incorrect. Do not take the medication more often than prescribed or in larger doses as it will not help you to get well faster, rather it will

increase the risk of side effects and pose further problems for you. The medication should not be stopped without the doctor's approval and it should be used regularly and at the same time each day for best results. If your condition remains static or deteriorates inform the doctor. The exact procedure that risperidone uses in order to be effective is not fully understood. However, just like other antipsychotics, it interferes with the communication between the nerves in the brain. Nerves communicate with each other when they make and release certain chemicals known as neurotransmitters. Neurotransmitters attach themselves to nerve receptors when they travel to nearby nerves. This attachment will either inhibit or activate the function of these nerves. Risperidone blocks the nerve receptors like dopamine type 2, serotonin type 2, and also the alpha 2 adrenergic receptors. Psychotic disorders are caused when communication between nerves in the brain becomes abnormal and alters the way neurotransmitters communicate. Risperidone works by altering this psychotic state. increased sensitivity of the skin to sunlight Herbal medications like St. John's wort could worsen sensitivity to the sun and could also increase serotonin when used with risperidone and so combining the two is not advisable. Ma huang and yohimbe are two other herbal remedies that should be avoided. Kava kava and valerian could increase drowsiness. Ginseng that works partly as an MAO inhibitor should not be combined with risperidone. Alcohol should not be imbibed while taking risperidone and smoking marijuana is not advisable either as sleepiness and inactivity could increase. Avoid exposure to the sun as the medication could lead to an increase in photosensitivity. Do not stop taking risperidone without first consulting the doctor. Store the medicine away from light and moisture, at room temperature. If you are using the oral solution of risperidone make sure it does not freeze. Do not store any medication in the bathroom and keep them out of reach of children and pets. Medicine should not be flushed down the toilet or poured into the drain unless advised to do so. Safe and proper disposal of medicine that is outdated or not needed should be carried out after consultation with the local waste disposal company or the pharmacist. Black cohosh is also not advised with Risperidone.

Efficacy and Safety

http://www.mentalhealth.com/mag1/scz/sb-risp.html December 09, 2014

Risperidone is the first antipsychotic marketed in the United States since clozapine. Introduced to the U.S. market in 1994, risperidone is a benzisoxazol derivative ...

Risperidone is the first antipsychotic marketed in the United States since clozapine. Introduced to the U.S. market in 1994, risperidone is a benzisoxazol derivative with combined dopamine D and serotonin 5HT receptor-blocking properties. Risperidone has a potency comparable to haloperidol as a D antagonist, but it has a much greater affinity for 5HT receptor sites. It also has relatively high affinity for alpha-adrenergic and histamine receptors in contrast to haloperidol.

No comprehensive review on risperidone has been published to date. This review addresses the following questions:

1. What is the efficacy and effectiveness (vs. placebo and/or older conventional antipsychotics) of risperidone during acute symptom episodes on the reduction of positive symptoms and negative/deficit symptoms, and on other outcomes?

2. What is the efficacy (vs. placebo and/or conventional antipsychotics) of risperidone during maintenance treatment on the reduction of positive symptoms and negative/deficit symptoms, and on other outcomes?

3. Is risperidone efficacious for patients with schizophrenia who fail to respond to conventional antipsychotics?

4. What are the side effects and risks associated with risperidone?

Computerized searches of MEDLINE and PSYCLIT were conducted back to 1988. In addition, the references in the articles that were obtained from the computerized searches were checked to ensure that relevant articles otherwise not identified were included. Only nine existing double-blind studies were selected for this review.

Owing to the small number of studies and the fact that all are acute treatment trials, the findings from each study are summarized. The characteristics of the studies and study samples are shown in tables 1 and 2, respectively. Table 3 summarizes the outcomes of each study. Following this are answers to the review questions.

Findings of the Studies.

Heinrich et al. (1994) compared two doses of risperidone with 400 mg of clozapine and found a similar reduction of scores on the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham 1962) in all three treatment groups. The percentage of patients rated "very much improved" or "much improved" on the Clinical Global Impressions (CGI; Guy 1976) scale was 60 percent for the 4-mg risperidone group, 42 percent for the 8-mg risperidone group, and 60 percent for the clozapine group. However, clozapine tended to cause more side effects than were observed in the two risperidone groups, especially in those patients taking 4 mg of risperidone. The investigators conclude that 4 mg of risperidone represents an effective alternative to clozapine based on its superior side effect profile. Unfortunately, this report does not indicate how many (if any) patients had a history of treatment refractoriness.

Borison et al. (1992) compared 2 to 10 mg of risperidone with 4 to 20 mg of haloperidol and placebo. They found a significant reduction of BPRS total scores in both the risperidone and the haloperidol group but no change in the placebo group. Fifty-eight percent of all patients in the risperidone group showed at least a 20-percent reduction of their BPRS total score, while only 25 percent of patients in the haloperidol group showed such a reduction. Risperidone also produced a superior result on the CGI: 83 percent of the risperidone group were rated as improved compared with 58 percent of the haloperidol group. Both treatments were significantly more effective than placebo. With regard to negative symptoms, no significant changes in scores on the Scale for the Assessment of Negative Symptoms (SANS; Andreasen 1984) were observed in any treatment group.

Claus et al.(1992) reported results that tended to favor risperidone over haloperidol. The risperidone group showed a significant improvement on the Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987) total score and the positive and general psychopathology subscale scores on the Schedule for Affective Disorders and Schizophrenia (SADS-C; Endicott and Spitzer 1978) total scale score, and on the Nurses' Observation Scale for Inpatient Evaluation (NOSIE-30; Guy 1976) total scale score, while the haloperidol group did not. Between-group differences were significant for the SADS-C but not for the PANSS total score, the PANSS positive symptom subscale score, or the NOSIE-30. There was, however, a statistical trend in favor of risperidone on the general psychopathology subscale of the PANSS. More patients in the risperidone group than in the haloperidol group (33% vs. 24%) were rated as showing "clinically significant" improvement (not defined by authors) on the PANSS total scores. Among patients with a high initial rating on the PANSS negative subscale at baseline, the proportion improving remained the same in the risperidone group (33%) but dropped to 13 percent in the haloperidol group.

The large European multicenter study (Müller-Spahn 1992) revealed a bell-shaped dose-response curve as measured

by the PANSS and the CGI; that is, 1 mg of risperidone proved to be least effective, the 4- and 8-mg doses showed an optimal response, and the 12- and 16-mg doses were less effective. A 20-mg dose of haloperidol was as effective as a 16-mg dose of risperidone. If only patients with initial high anxiety/depression scores are considered, 4 and 8 mg of risperidone proved to be significantly better than haloperidol on a number of outcomes, including the PANSS and BPRS total scores, the PANSS general psychopathology subscale, the BPRS activity and anxiety/depression clusters, and the percentage of patients reaching clinical improvement on the PANSS and BPRS. In the high anxiety/depression subgroup, haloperidol lost the superiority over 1 mg of risperidone evident in the intention-to-treat analysis. Results for the patients with low anxiety/depression scores were not given.

Similar results were found in the two North American multicenter studies (Chouinard et al. 1993; Marder and Meibach 1994). Using the percentage of patients with a reduction of the PANSS total score greater than 20 percent as their primary outcome measure, the Canadian study (Chouinard et al. 1993) found that 6 mg of risperidone led to the highest rate of responders (73%). This was significantly better than placebo (14%) but not better than 20 mg of haloperidol (48%). Risperidone doses of 2 and 16 mg also showed significantly higher rates of responders than placebo.

In the U.S. study (Marder and Meibach 1994), significantly more patients in the risperidone 6-, 10-, and 16-mg groups were classified as responders (57%, 40%, and 51%, respectively) than in the placebo group (22%). When compared with the 20-mg haloperidol group, which had a response rate of 30 percent, significantly more patients in the risperidone 6- and 16-mg groups were classified as responders. When using the response criteria defined by Kane et al. (1988),1 only the 6-mg group showed a significantly higher response rate than the 20-mg haloperidol group (41% in the 6-mg

risperidone group vs. 22% in the haloperidol group).

1In both North American studies, a post-hoc analysis also used as a criterion for response a 20-percent reduction on the PANSS-derived BPRS total score -- either a CGI severity of illness score less than 3 or a (PANSS-derived) BPRS total score less than 35.

On changes in PANSS total scores, 6 mg of risperidone proved significantly better than 20 mg of haloperidol in the study by Chouinard et al. (1993), while Marder and Meibach (1994) found both 6 and 16 mg of risperidone to have superiority over 20 mg of haloperidol. Six milligrams of risperidone in the Canadian study (Chouinard et al. 1993) and 6 and 16 mg of risperidone in the U.S. study (Marder and Meibach 1994) were also found to be significantly better than placebo on the positive and negative symptom subscale of the PANSS. In the Canadian study (Chouinard et al. 1993), all active treatments were found to be significantly better than placebo on change of the CGI. Six milligrams of risperidone tended to be better than 20 mg of haloperidol. On the same outcome measure, the U.S. study (Marder and Meibach 1994) found all active treatments with the exception of 2 mg of risperidone to be significantly better than placebo. In both studies, the 6-, 10-, and 16-mg risperidone groups and the 20-mg haloperidol group showed significantly higher rates of improved patients as rated on the CGI scale than did the placebo group (Chouinard et al. 1993; Marder and Meibach 1994). In addition, in the Chouinard et al. (1993) study, significantly more patients were classified as improved in the 6-mg risperidone group than in the 20-mg haloperidol group.

The study by Ceskova and Svestka (1993) comparing 2 to 20 mg of risperidone with 2 to 20 mg of haloperidol (mean maximal dose = 9.9 mg; mean minimal dose = 2.9 mg) found similar efficacy for the two treatments. In the risperidone group, 45 percent of the patients showed a very good response and 32 percent showed a partial response, while the corresponding results for haloperidol were 45 and 42 percent, respectively. Both treatments led to a statistically significant reduction of BPRS total scores with no between-group differences. The haloperidol groups showed significantly lower scores on BPRS anxiety and depression items (and on the anxiety/depression factor) than the risperidone group.

The study by Hoyberg et al. (1993) used perphenazine as the comparison drug. The mean daily treatment doses were 8.5 mg for risperidone and 28 mg for perphenazine. The two treatments were equally effective in reducing PANSS total scores, negative and positive symptom subscale scores, and PANSS-derived BPRS factor scores. Only on the BPRS hostility factor did risperidone lead to a significantly greater improvement than perphenazine. When clinical improvement was defined as a 20 percent reduction of the PANSS total scores, there was no significant group difference. However, when a 20-percent BPRS reduction is used as the criterion for response, the rate is slightly higher in the risperidone group (78%) and significantly different from the perphenazine treatment group. On the CGI, improvement scores between the two groups did not significantly differ.

In a post-hoc analysis, the authors divided the study patients into "negative" or "positive" subtypes, depending on whether the patients showed higher scores on the PANSS negative or positive symptom subscales. Among the positive subtype patients, the two treatments fared equally. Among the negative subtype patients, the percentage of patients rated as responding (using 20-percent reduction of either PANSS or BPRS total scores as the criterion) was significantly higher in the risperidone than in the perphenazine group. Also, risperidone led to a significantly greater improvement on the BPRS hostility factor.

Finally, the study by Min et al. (1993) using a "semi-fixed" dosage did not find any significant differences between risperidone and haloperidol on reductions of PANSS total score and positive and negative symptom subscale scores, on PANSS-derived BPRS factor scores, and on CGI severity of illness ratings.

What Is the Efficacy and Effectiveness of Risperidone (vs. Placebo and/or Older Conventional Antipsychotics) During Acute Symptom Episodes on the Reduction of Positive Symptoms and Negative/Deficit Symptoms, and on Other Outcomes? The studies reviewed demonstrate equivalent if not superior efficacy of risperidone compared with haloperidol and perphenazine in the treatment of schizophrenia patients. The available data appear to indicate that 4 to 8 mg is the most effective dose for risperidone. This range is based on both fixed-and adjusted-dose studies.

The finding by Marder and Meibach (1994) that 16 mg is as effective as 6 mg may indicate that for certain patients, a higher dose is required to get the full benefit of the treatment. Given the heterogeneity of the patients included in these trials, further analyses (or additional studies) focusing on both refractory

and more acute subgroups may be helpful in targeting dosages to specific patient subgroups. However, in view of the finding discussed below that risperidone in dosages of less than 10 to 12 mg produces significantly fewer extrapyramidal symptoms (EPS), an initial dose range between 4 and 8 mg seems reasonable. If a patient does not show improvement after 3 to 4 weeks, an increase to a higher dose can be considered.

It has been suggested that risperidone may have a special role in the treatment of negative symptoms. Claus et al. (1992) found clinically significant improvement in 33 percent of the total risperidone group as well as in 33 percent of the subgroup of patients with high negative symptom scores at baseline. The corresponding data for haloperidol were 33 percent for all patients but only 13 percent for patients with predominantly negative symptoms. In the Canadian study (Chouinard et al. 1993) and the U.S. multicenter study (Marder and Meibach 1994), it was found that 6 mg (in both studies) and 10 and 16 mg (in the U.S. study only) of risperidone were significantly better than placebo in reducing negative symptoms, whereas 20 mg of haloperidol was not. Because EPS easily can be rated as negative symptoms, it will be important for future research to determine whether this finding reflects lower symptoms of EPS for risperidone in doses below 10 mg.

Similarly interesting is the finding of Hoyberg et al. (1993) that among patients with higher ratings of negative than positive symptoms on the PANSS subscales, the rate of responders was significantly higher in the risperidone than in the perphenazine group. Again, however, this is difficult to interpret since a decrease in EPS in the risperidone group could have contributed to this result. Such a possibility was not addressed by the authors by, for example, covarying for change in EPS during treatment or baseline EPS. Also, the authors' criteria for assigning patients to a positive or negative subgroup only determined the relative predominance of negative or positive symptoms and did not necessarily indicate that a given patient scored high or low on the positive or negative symptom subscales. For this reason, it is unclear whether the negative subtype patients in fact have a deficit state.

Another target population for risperidone may be patients with prominent symptoms of anxiety and depression. The European multicenter study (Müller-Spahn 1992) found that among this subgroup, risperidone in doses of 4 and 8 mg proved to be significantly superior to 10 mg of haloperidol.

No data are available at this point to determine the effectiveness of risperidone.

What Is the Efficacy of Risperidone (vs. Placebo and/or Conventional Antipsychotics) During Maintenance Treatment on the Reduction of Positive Symptoms and Negative/Deficit Symptoms, and on Other Outcomes? To date, no double-blind studies using risperidone for maintenance treatment have been reported.

Is Risperidone Efficacious for Patients With Schizophrenia Who Fail to Respond to Conventional Antipsychotics? There are no published reports of studies in well-characterized treatment-refractory patients. Of particular interest would be comparisons with clozapine, as well as trials in schizoaffective patients and in patients selected for predominant negative/deficit symptoms.

What Are the Side Effects and Risk Associated With Risperidone? A consistent finding across all studies is that risperidone below 10 mg/day did not produce more EPS than placebo. Risperidone at 16 mg produced as much EPS as 20 mg of haloperidol in the U.S. multicenter study (Marder and Meibach 1994) but not in the Canadian study (Chouinard et al. 1993), which found 10 mg to cause the most EPS among the different risperidone doses. However, like all studies reporting on this factor, Chouinard et al. (1993) found that the use of anticholinergic medication was significantly higher in the 20-mg haloperidol group than in any risperidone group. Also, a linear relationship between risperidone dose and EPS scores was found in both the European and Canadian multicenter studies. In the study by Min et al. (1993), in which risperidone was compared with equal dose ranges of haloperidol, risperidone treatment was not associated with a greater decrease of the global EPS rating as compared with haloperidol. Only on certain subitems and subscores was there a trend in favor or risperidone. Overall, it seems justified to conclude that, in general, doses below 10 mg are less likely to cause EPS than doses above 10 mg. However, more work is needed in this area.

At the recommended dose of 6 mg, risperidone appears to be well tolerated. The adverse effects most commonly associated with treatment discontinuation in the US and Canadian studies were dizziness (1.5%), nausea (1.2%), and agitation (1.0%). The most common adverse effects among patients receiving 10 mg/day or less of risperidone in the North American studies were insomnia (26%), agitation (22%), EPS (17%), headache (17%), anxiety (12%), and rhinitis F(10%). In most cases, these rates did

not differ significantly from those for placebo, but 6 mg of risperidone did produce significantly fewer EPS than 20 mg of haloperidol.

Risperidone is a potent alpha-adrenergic antagonist. Therefore, it is important to closely follow blood pressure early in treatment to evaluatefor the presence of postural hyppotension. To date, no confirmed cases of neuroleptic malignant syndrome or tardive dyskinesia have occurred in association with risperidone. However, more long-term experience is necessary before drawing any conclusions on these sequelae.

In the study by Hoyberg et al. (1993), a high percentage of patients on risperidone were noted to show "asthenia" (49% vs. 28% in the perphenazine group) and weight gain (52% vs. 24% in the perphenazine group). A moderate increase in body weight (mean of 2.3 kg over an average period of 7.4 months) has been reported and is likely due to the drug's antagonism of serotonin receptors. Risperidone is also associated with significant increases in prolactin. However, it does not appear to produce hypersalivation, persistent tachycardia, cataplexy, myoclonus, or seizures.

The large-scale clinical trials conducted with risperidone demonstrate its antipsychotic efficacy to be consistently superior to that of placebo and at least comparable to that of haloperidol and perphenazine. The extend to which risperidone might be considered superior to haloperidol rests on the interpretation of the existing data base. The majority of studies conducted used multiple fixed doses of risperidone and one fixed dose of haloperidol. The analyses in which risperidone was found to be superior to haloperidol were by and large conducted with the optimal dose of risperidone. In the one study (Min et al. 1993) in which risperidone was compared with a similar dose of haloperidol, and in the European multicenter study (Müller-Spahn 1992) in which fixed doses of risperidone were compared with 10 mg of haloperidol, risperidone was not found to show superior efficacy. One could therefore argue that, before concluding that risperidone is superior to haloperidol, haloperidol should be used in more than one fixed dose as well. Despite the fact that haloperidol has been widely used for more than two decades, debate continues as to what dosage is optimal. The issue is important not purely from an efficacy standpoint but also with regard to adverse effects, given that EPS can easily be mistaken for, or add to negative symptoms or tension and agitation.

Risperidone shares some receptor-binding proportions with clozapine but not with other drugs. Whether risperidone will prove to be as useful as clozapine in treatment-refractory patients remains to be seen. Studies are being planned to compare risperidone directly with clozapine in refractory patients.

How much of an advance does risperidone represent? To some extent, this question is difficult to answer until we have more experience with the drug. At the recommended dosage of 6 mg/day, it appears to produce fewer EPS than haloperidol at a dosage of 20 mg/day and not significantly more EPS than seen in the placebo control group. Whether 6 mg/day will prove to be the optimal dosage for the general population of patients with acute episodes or exacerbations remains to be determined. If higher doses are required, the advantages in terms of EPS may disappear. As previously mentioned, data need to be generated in deficity-state patients or patients with predominant persistent negative symptoms as well as in treatment-refractory patients. Such studies will help to identify risperidone's appropriate place in the treatment of schizophrenia.

It is clear that the marketing of this drug has tapped into a potentially large, pent-up demand for new antipsychotic drugs. How the compound succeeds, particularly in this era of cost containment, will depend on whether initial expectations are realized in routine clinical practice.

In conclusion, research questions that remain to be answered include the following:

1. What is the efficacy of risperidone in treating deficit symptoms?

2. What is the effectiveness of risperidone in typical clinical treatment settings?

3. Is risperidone an effective maintenance therapy?

4. Is risperidone efficacious among patients with illness refractory to conventional antipsychotics?

5. What is the cost-effectiveness of risperidone relative to conventional antipsychotics and clozapine, taking into consideration impacts on positive and negative symptoms, side effects, enhancement of functional status, quality of life, and costs?

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RISPERDAL - Janssen Pharmaceutica

http://www.janssenpharmaceuticalsinc.com/assets/risperdal.pdf December 09, 2014

1 RISPERDAL® (risperidone) HigHligHts of Prescribing information these highlights do not include all the information needed to use ris® PerDal

RISPERDAL® Revised: 04/2014-
RISPERDAL® (risperidone)
(risperidone) 015036-140508

---------- Warnings and Precautions----------
Highlights of Prescribing Information •
Cerebrovascular events, including stroke, in elderly patients with dementia-
These highlights do not include all the information needed to use RISPERDAL®
related psychosis: R ISPERDAL® is not approved for use in patients with
safely and effectively. See full prescribing information for RISPERDAL®.
dementia-related psychosis. (5.2)
RISPERDAL® (risperidone) tablets, for oral use •
Neuroleptic Malignant Syndrome: Manage with immediate discontinuation of
RISPERDAL® (risperidone) oral solution-
RISPERDAL® and close monitoring. (5.3)
RISPERDAL® M-TAB® (risperidone) orally disintegrating tablets •
Tardive dyskinesia: Consider discontinuing RISPERDAL® if clinically indicated.

(5.4)
Initial U.S. Approval: 1993
•
Metabolic Changes: Atypical antipsychotic drugs have been associated with

metabolic changes that may increase cardiovascular/ cerebrovascular risk.
WARNING:
These metabolic changes include hyperglycemia, dyslipidemia, and weight
INCREASED MORTALITY IN ELDERLY PATIENTS WITH
gain. (5.5)
DEMENTIA-RELATED PSYCHOSIS

o Hyperglycemia and Diabetes Mellitus: Monitor patients for symptoms of
See full prescribing information for complete boxed warning.

hyperglycemia including polydipsia, polyuria, polyphagia, and weakness.
• Elderly patients with dementia-related psychosis treated with
Monitor glucose regularly in patients with diabetes or at risk for diabetes.
antipsychotic drugs are at an increased risk of death.
(5.5)
• RISPERDAL® is not approved for use in patients with dementia-related
psychosis. (5.1)
o Dyslipidemia: Undesirable alterations have been observed in patients

treated with atypical antipsychotics. (5.5)

o Weight Gain: Significant weight gain has been reported. Monitor weight
---------- Indications and Usage----------
gain. (5.5)
RISPERDAL® is an atypical antipsychotic indicated for: •
Hyperprolactinemia: Prolactin elevations occur and persist during chronic
• Treatment of schizophrenia (1.1)
administration. (5.6)
• As monotherapy or adjunctive therapy with lithium or valproate, for the
• Orthostatic hypotension: For patients at risk, consider a lower starting dose
treatment of acute manic or mixed episodes associated with Bipolar I
and slower titration. (5.7)
Disorder (1.2) •

Leukopenia, Neutropenia, and Agranulocytosis: Perform complete blood
• Treatment of irritability associated with autistic disorder (1.3)
counts in patients with a history of clinically significant low white blood cell

count (WBC). Consider discontinuing RISPERDAL® if a clinically significant
----------DOSAGE AND ADMINISTRATION----------
decline in WBC occurs in the absence of other causative factors. (5.8)
• Recommended daily dosage:
• Potential for cognitive and motor impairment: Use caution when operating

	Initial Dose	Target Dose	Effective Dose Range

machinery. (5.9)
• Seizures: Use cautiously in patients with a history of seizures or with

Schizophrenia: adults (2.1)	2 mg	4 to 8 mg	4 to 16 mg

conditions that lower the seizure threshold. (5.10)

Schizophrenia: adolescents (2.1)	0.5 mg	3 mg	1 to 6 mg

----------Adverse Reactions----------

Bipolar mania: Adults (2.2)	2 to 3 mg	1 to 6 mg	1 to 6 mg

The most common adverse reactions in clinical trials (>5% and twice placebo)

Bipolar mania: in children and adolescents (2.2)	0.5 mg	1 to 2.5 mg	1 to 6 mg

were parkinsonism, akathisia, dystonia, tremor, sedation, dizziness, anxiety,
blurred vision, nausea, vomiting, upper abdominal pain, stomach discomfort,

dyspepsia, diarrhea, salivary hypersecretion, constipation, dry mouth, increased

Irritability associated with autistic disorder (2.3)	0.25 mg (Weight < 20 kg)	0.5 mg (<20 kg)	0.5 to 3 mg

appetite, increased weight, fatigue, rash, nasal congestion, upper respiratory
tract infection, nasopharyngitis, and pharyngolaryngeal pain. (6)

	0.5 mg (Weight ≥20 kg)	1 mg (≥20 kg)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Pharmaceuticals,
Inc. at 1-800-JANSSEN (1-800-526-7736) or FDA at 1-800-FDA-1088 or

www.fda.gov/medwatch
• Severe Renal or Hepatic Impairment in Adults: Use a lower starting dose of
0.5 mg twice daily. May increase to dosages above 1.5 mg twice daily at
---------- Drug Interactions----------
intervals of at least one week. (2.4)
Carbamazepine and other enzyme inducers decrease plasma concentrations
• Oral Solution: Can be administered directly from calibrated pipette or mixed
of risperidone. Increase the RISPERDAL® dose up to double the patient's usual
with beverage (water, coffee, orange juice, or low-fat milk). (2.6)
dose. Titrate slowly. (7.1)
• M-TAB Orally Disintegrating Tablets: Open the blister only when ready to
• Fluoxetine, paroxetine, and other CYP 2D6 enzyme inhibitors increase plasma
administer, and immediately place tablet under tongue. Can be swallowed
concentrations of risperidone. Reduce the initial dose. Do not exceed a final
with or without liquid. (2.7)
dose of 8 mg per day of RISPERDAL®. (7.1)

----------Dosage Forms and Strengths----------
---------- Use in specific Populations----------
• Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg (3)
• Pregnancy: Based on animal data, may cause fetal harm. (8.1)
• Oral solution: 1 mg per mL (3)
• Nursing Mothers: Discontinue drug or nursing, taking into consideration the

importance of drug to the mother. (8.3)
• Orally disintegrating tablets: 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg (3)
----------Contraindications----------
See 17 for PATIENT COUNSELING INFORMATION
• Known hypersensitivity to RISPERDAL® (4)
Revised: 04/2014

1

RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)

Full Prescribing Information: Contents*

FULL PRESCRIBING INFORMATION

WARNING:

INCREASED MORTALITY IN ELDERLY PATIENTS WITH-
DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. RISPERDAL® (risperidone) is not approved for the treatment of patients with dementia-related psychosis. [See Warnings and Precautions (5.1)]-

1 Indications and Usage

1.1 Schizophrenia

RISPERDAL® (risperidone) is indicated for the treatment of schizophrenia.

1.2 Bipolar Mania

Monotherapy

RISPERDAL® is indicated for the treatment of acute manic or mixed episodes associated with Bipolar I Disorder. Efficacy was established in 2 short-term trials in adults and one short-term trial in children and adolescents (ages 10 to 17 years) [see Clinical Studies (14.2)].

Adjunctive Therapy

RISPERDAL® adjunctive therapy with lithium or valproate is indicated for the treatment of acute manic or mixed episodes associated with Bipolar I Disorder. Efficacy was established in one short-term trial in adults [see Clinical Studies (14.3)].

1.3 Irritability Associated with Autistic Disorder

RISPERDAL® is indicated for the treatment of irritability associated with autistic disorder, including symptoms of aggression towards others, deliberate self-injuriousness, temper tantrums, and quickly changing moods. Efficacy was established in 3 short-term trials in children and adolescents (ages 5 to 17 years) [see Clinical Studies (14.4)].

2

RISPERDAL® (risperidone)-

RISPERDAL® (risperidone)

2 Dosage and Administration

2.2 Bipolar Mania

Table 1. Recommended Daily Dosage by Indication

	Initial Dose	Titration (Increments)	Target Dose	Effective Dose Range	Usual Dose
Adults					
Schizophrenia: adults (2.1)	2 mg	1 to 2 mg	4 to 8 mg	4 to 16 mg	
Schizophrenia: adolescents (2.2)	0.5 mg	0.5 to 1 mg	3 mg	1 to 6 mg	
Pediatrics					
Bipolar mania:	2 to 3 mg	1 mg	1 to 6 mg	1 to 6 mg	

The initial dose range is 2 mg to 3 mg per day. The dose may be adjusted at intervals of 24 hours or greater, in increments of 1 mg per day. The effective dose range is 1 mg to 6 mg per day, as studied in the short-term, placebo-controlled trials. In these trials, short-term (3 week) anti-manic efficacy was demonstrated in a flexible dosage range of 1 mg to 6 mg per day [see Clinical Studies (14.2, 14.3)]. RISPERDAL® doses higher than 6 mg per day were not studied.

initial dose is 0.5 mg once daily, administered as a single-daily dose in the
adults (2.2)
morning or evening. The dose may be adjusted at intervals of 24 hours or greater,
Bipolar mania: 0.5 mg 0.5 to 1 mg 1 to 2.5 mg 1 to 6 mg in
increments of 0.5 mg or 1 mg per day, as tolerated, to the recommended target
children and
dose of 1 mg to 2.5 mg per day. Although efficacy has been demonstrated in
adolescents (2.2)
studies of pediatric patients with bipolar mania at doses between 0.5 mg and
Irritability in 0.25 mg After Day 4, at 0.5 mg: 0.5 to 3 mg 6
mg per day, no additional benefit was observed above 2.5 mg per day, and
autistic disorder Can increase to intervals of (body
higher doses were associated with more adverse events. Doses higher than
(2.3) 0.5 mg by Day 4: > 2 weeks: weight less
6 mg per day have not been studied.
(body weight 0.25 mg than 20 kg)
Patients experiencing persistent somnolence may benefit from administering half
less than 20 kg) (body weight
the daily dose twice daily.
less than 20 kg) 1 mg:
Maintenance Therapy
0.5 mg (body

There is no body of evidence available from controlled trials to guide a clinician
Can increase to 0.5 mg weight
in
the longer-term management of a patient who improves during treatment of an
1 mg by Day 4: (body weight greater than
acute manic episode with RISPERDAL®. While it is generally agreed that
(body weight greater than or or equal to
pharmacological treatment beyond an acute response in mania is desirable, both
greater than or equal to 20 kg) 20 kg)
for maintenance of the initial response and for prevention of new manic
equal to 20 kg)
episodes, there are no systematically obtained data to support the use of
-
RISPERDAL® in such longer-term treatment (i.e., beyond 3 weeks). The physician
Severe Renal and Hepatic Impairment in Adults: use a lower starting dose of
who
elects to use RISPERDAL® for extended periods should periodically
0.5 mg twice daily. May increase to dosages above 1.5 mg twice daily at intervals

re-evaluate the long-term risks and benefits of the drug for the individual patient.
of one week or longer.

2.3 Irritability Associated with Autistic Disorder — Pediatrics (Children and
2.1 Schizophrenia

Adolescents)
Adults
The dosage of RISPERDAL® should be individualized according to the response
Usual Initial Dose and
tolerability of the patient. The total daily dose of RISPERDAL® can be
RISPERDAL® can be administered once or twice daily. Initial dosing is 2 mg per
administered once daily, or half the total daily dose can be administered
day. May increase the dose at intervals of 24 hours or greater, in increments of
twice daily.
1 to 2 mg per day, as tolerated, to a recommended dose of 4 to 8 mg per day. In
For patients with body weight less than 20 kg, initiate dosing at 0.25 mg per day.
some patients, slower titration may be appropriate. Efficacy has been
For patients with body weight greater than or equal to 20 kg, initiate dosing at
demonstrated in a range of 4 mg to 16 mg per day. However, doses above 6 mg
0.5 mg per day. After a minimum of four days, the dose may be increased to the
per day for twice daily dosing were not demonstrated to be more efficacious
recommended dose of 0.5 mg per day for patients less than 20 kg and 1.0 mg per
than lower doses, were associated with more extrapyramidal symptoms and
day for patients greater than or equal to 20 kg. Maintain this dose for a minimum
other adverse effects, and are generally not recommended. In a single study of
14 days. In patients not achieving sufficient clinical response, the dose may be
supporting once-daily dosing, the efficacy results were generally stronger for
increased at intervals of 2 weeks or greater, in increments of 0.25 mg per day for
8 mg than for 4 mg. The safety of doses above 16 mg per day has not been
patients less than 20 kg, or increments of 0.5 mg per day for patients greater than
evaluated in clinical trials [see Clinical Studies (14.1)]. or

equal to 20 kg. The effective dose range is 0.5 mg to 3 mg per day. No dosing
Adolescents
data are available for children who weigh less than 15 kg.
The initial dose is 0.5 mg once daily, administered as a single-daily dose in the
Once sufficient clinical response has been achieved and maintained, consider
morning or evening. The dose may be adjusted at intervals of 24 hours or greater,
gradually lowering the dose to achieve the optimal balance of efficacy and
in increments of 0.5 mg or 1 mg per day, as tolerated, to a recommended dose of
safety. The physician who elects to use RISPERDAL® for extended periods
3 mg per day. Although efficacy has been demonstrated in studies of adolescent
should periodically re-evaluate the long-term risks and benefits of the drug for
patients with schizophrenia at doses between 1 mg to 6 mg per day, no the
individual patient.
additional benefit was observed above 3 mg per day, and higher doses were
Patients experiencing persistent somnolence may benefit from a once-daily dose
associated with more adverse events. Doses higher than 6 mg per day have not
administered at bedtime or administering half the daily dose twice daily, or a
been studied.
reduction of the dose.
Patients experiencing persistent somnolence may benefit from administering half 2.4
Dosing in Patients with Severe Renal or Hepatic Impairment
the daily dose twice daily. For
patients with severe renal impairment (CLcr < 30 mL/min) or hepatic
Maintenance Therapy
impairment (10-15 points on Child Pugh System), the initial starting dose is 0.5 mg
While it is unknown how long a patient with schizophrenia should remain on
twice daily. The dose may be increased in increments of 0.5 mg or less,
RISPERDAL®, the effectiveness of RISPERDAL® 2 mg per day to 8 mg per day at
administered twice daily. For doses above 1.5 mg twice daily, increase in
delaying relapse was demonstrated in a controlled trial in adult patients who had
intervals of one week or greater [see Use in Specific Populations (8.6 and 8.7)].
been clinically stable for at least 4 weeks and were then followed for a period of 2.5
Dose Adjustments for Specific Drug Interactions
1 to 2 years [see Clinical Studies (14.1)]. Both adult and adolescent patients who When-
RISPERDAL® is co-administered with enzyme inducers (e.g.,
respond acutely should generally be maintained on their effective dose beyond
carbamazepine), the dose of RISPERDAL® should be increased up to double the
the acute episode. Patients should be periodically reassessed to determine the
patient’s usual dose. It may be necessary to decrease the RISPERDAL® dose
need for maintenance treatment.
when enzyme inducers such as carbamazepine are discontinued [see Drug
Reinitiation of Treatment in Patients Previously Discontinued
Interactions (7.1)]. Similar effect may be expected with co-administration of
-
RISPERDAL® with other enzyme inducers (e.g., phenytoin, rifampin, and
Although there are no data to specifically address reinitiation of treatment, it is

phenobarbital).
recommended that after an interval off RISPERDAL®, the initial titration schedule
should be followed.
When fluoxetine or paroxetine is co-administered with RISPERDAL®, the dose of
-
RISPERDAL® should be reduced. The RISPERDAL® dose should not exceed 8 mg
Switching From Other Antipsychotics per
day in adults when co-administered with these drugs. When initiating
There are no systematically collected data to specifically address switching
therapy, RISPERDAL® should be titrated slowly. It may be necessary to increase
schizophrenic patients from other antipsychotics to RISPERDAL®, or treating the-
RISPERDAL® dose when enzyme inhibitors such as fluoxetine or paroxetine
patients with concomitant antipsychotics.
are discontinued [see Drug Interactions (7.1)].

3

RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)
2.6 Administration of RISPERDAL® Oral Solution
5.2 Cerebrovascular Adverse Reactions, Including Stroke, in Elderly Patients
ISPERDAL® Oral Solution can be administered directly from the calibrated
R
with Dementia-Related Psychosis
pipette, or can be mixed with a beverage prior to administration. RISPERDAL®
Cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack),
Oral Solution is compatible in the following beverages: water, coffee, orange

including fatalities, were reported in patients (mean age 85 years; range 73-97)
juice, and low-fat milk; it is NOT compatible with either cola or tea.
in trials of risperidone in elderly patients with dementia-related psychosis.
2.7 Directions for Use of RISPERDAL® M-TAB® Orally Disintegrating Tablets
In placebo-controlled trials, there was a significantly higher incidence

of cerebrovascular adverse events in patients treated with risperidone
Tablet Accessing

compared to patients treated with placebo. RISPERDAL® is not approved for the
RISPERDAL® M-TAB® Orally Disintegrating Tablets 0.5 mg, 1 mg, and 2 mg

treatment of patients with dementia-related psychosis. [see Boxed Warning and
RISPERDAL® M-TAB® Orally Disintegrating Tablets 0.5 mg, 1 mg, and 2 mg are
Warnings and Precautions (5.1)]
supplied in blister packs of 4 tablets each.

5.3 Neuroleptic Malignant Syndrome
Do not open the blister until ready to administer. For single tablet removal,
separate one of the four blister units by tearing apart at the perforations. Bend
Antipsychotic drugs including RISPERDAL® can cause a potentially fatal
the corner where indicated. Peel back foil to expose the tablet. DO NOT push the
symptom complex referred to as Neuroleptic Malignant Syndrome (NMS).
tablet through the foil because this could damage the tablet.
Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered

mental status, and autonomic instability (irregular pulse or blood pressure,
RISPERDAL® M-TAB® Orally Disintegrating Tablets 3 mg and 4 mg
tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include
RISPERDAL® M-TAB® Orally Disintegrating Tablets 3 mg and 4 mg are supplied in
elevated creatine phosphokinase (CPK), myoglobinuria, rhabdomyolysis, and
a child-resistant pouch containing a blister with 1 tablet each.
acute renal failure.
The child-resistant pouch should be torn open at the notch to access the blister.
The diagnostic evaluation of patients with this syndrome is complicated. In
Do not open the blister until ready to administer. Peel back foil from the side to
arriving at a diagnosis, it is important to identify cases in which the clinical
expose the tablet. DO NOT push the tablet through the foil, because this could
presentation includes both serious medical illness (e.g., pneumonia, systemic
damage the tablet.
infection, etc.) and untreated or inadequately treated extrapyramidal signs and
Tablet Administration
symptoms (EPS). Other important considerations in the differential diagnosis
Using dry hands, remove the tablet from the blister unit and immediately place
include central anticholinergic toxicity, heat stroke, drug fever, and primary
the entire R ISPERDAL® M-TAB® Orally Disintegrating Tablet on the tongue. The
central nervous system pathology.
RISPERDAL® M-TAB® Orally Disintegrating Tablet should be consumed
The management of NMS should include: (1) immediate discontinuation of
immediately, as the tablet cannot be stored once removed from the blister unit.
antipsychotic drugs and other drugs not essential to concurrent therapy;
RISPERDAL® M-TAB® Orally Disintegrating Tablets disintegrate in the mouth
(2) intensive symptomatic treatment and medical monitoring; and (3) treatment
within seconds and can be swallowed subsequently with or without liquid.
of any concomitant serious medical problems for which specific treatments are
Patients should not attempt to split or to chew the tablet.
available. There is no general agreement about specific pharmacological
3 Dosage Forms and Strengths
treatment regimens for uncomplicated NMS.
RISPERDAL® Tablets are available in the following strengths and colors: 0.25 mg
If a patient requires antipsychotic drug treatment after recovery from NMS, the
(dark yellow), 0.5 mg (red-brown), 1 mg (white), 2 mg (orange), 3 mg (yellow), and
potential reintroduction of drug therapy should be carefully considered. The
4 mg (green). All are capsule shaped, and imprinted with “JANSSEN” on one
patient should be carefully monitored, since recurrences of NMS have been
side and either “Ris 0.25”, “Ris 0.5”, “R1”, “R2”, “R3”, or “R4” on the other side
reported.
according to their respective strengths.
5.4 Tardive Dyskinesia
RISPERDAL® Oral Solution is available in a 1 mg/mL strength.
A syndrome of potentially irreversible, involuntary, dyskinetic movements may
RISPERDAL® M-TAB® Orally Disintegrating Tablets are available in the following
develop in patients treated with antipsychotic drugs. The risk of developing
strengths, colors, and shapes: 0.5 mg (light coral, round), 1 mg (light coral,

tardive dyskinesia and the likelihood that it will become irreversible are believed square), 2 mg (coral, square), 3 mg (coral, round), and 4 mg (coral, round). All to increase as the duration of treatment and the total cumulative dose of are biconvex and etched on one side with “R0.5”, “R1”, “R2”, “R3”, or “R4” antipsychotic drugs administered to the patient increase. However, the syndrome according to their respective strengths. can develop, although much less commonly, after relatively brief treatment

periods at low doses.

4 Contraindications

There is no known treatment for established cases of tardive dyskinesia, RISPERDAL® is contraindicated in patients with a known hypersensitivity to

although the syndrome may remit, partially or completely, if antipsychotic RISPERDAL®. Hypersensitivity reactions, including anaphylactic reactions and

treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress angioedema, have been observed in patients treated with risperidone.

(or partially suppress) the signs and symptoms of the syndrome and thereby may

5 Warnings and Precautions

possibly mask the underlying process. The effect that symptomatic suppression

5.1 Increased Mortality in Elderly Patients with Dementia-Related Psychosis

has upon the long-term course of the syndrome is unknown.

Elderly patients with dementia-related psychosis treated with antipsychotic

Given these considerations, prescribe RISPERDAL® in a manner that is most drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials

likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic (modal duration of 10 weeks), largely in patients taking atypical antipsychotic

treatment should generally be reserved for patients who suffer from a chronic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7

illness that: (1) is known to respond to antipsychotic drugs, and (2) for whom times the risk of death in placebo-treated patients. Over the course of a typical

alternative, equally effective, but potentially less harmful treatments are not 10-week controlled trial, the rate of death in drug-treated patients was about

available or appropriate. In patients who do require chronic treatment, the 4.5%, compared to a rate of about 2.6% in the placebo group. Although the

smallest dose and the shortest duration of treatment producing a satisfactory causes of death were varied, most of the deaths appeared to be either

clinical response should be sought. The need for continued treatment should be cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia)

reassessed periodically. in nature. Observational studies suggest that, similar to atypical antipsychotic

If signs and symptoms of tardive dyskinesia appear in a patient treated with drugs, treatment with conventional antipsychotic drugs may increase mortality.-

RISPERDAL®, consider drug discontinuation. However, some patients may The extent to which the findings of increased mortality in observational studies

require treatment with RISPERDAL® despite the presence of the syndrome. may be attributed to the antipsychotic drug as opposed to some characteristic(s)

of the patients is not clear.

5.5 Metabolic Changes

In two of four placebo-controlled trials in elderly patients with dementia-related

Atypical antipsychotic drugs have been associated with metabolic changes that psychosis, a higher incidence of mortality was observed in patients treated with

may increase cardiovascular/cerebrovascular risk. These metabolic changes furosemide plus RISPERDAL® when compared to patients treated with

include hyperglycemia, dyslipidemia, and body weight gain. While all of the RISPERDAL® alone or with placebo plus furosemide. No pathological mechanism

drugs in the class have been shown to produce some metabolic changes, each has been identified to explain this finding, and no consistent pattern for cause of

drug has its own specific risk profile. death was observed.

Hyperglycemia and Diabetes Mellitus

RISPERDAL® (risperidone) is not approved for the treatment of dementia-related

Hyperglycemia and diabetes mellitus, in some cases extreme and associated psychosis [see Boxed Warning].

with ketoacidosis or hyperosmolar coma or death, have been reported in

patients treated with atypical antipsychotics including RISPERDAL®. Assessment

of the relationship between atypical antipsychotic use and glucose abnormalities

4
RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)
is complicated by the possibility of an increased background risk of diabetes Table
4. Change in Random Lipids from Seven Placebo-Controlled, 3- to
mellitus in patients with schizophrenia and the increasing incidence of diabetes
8-Week, Fixed- or Flexible-Dose Studies in Adult Subjects with
mellitus in the general population. Given these confounders, the relationship
Schizophrenia or Bipolar Mania
between atypical antipsychotic use and hyperglycemia-related adverse events is-
RISPERDAL®
not completely understood. However, epidemiological studies suggest an
Placebo 1-8 mg/day >8-16 mg/day
increased risk of treatment-emergent hyperglycemia-related adverse events in
Mean change from baseline (mg/dL)
patients treated with the atypical antipsychotics. Precise risk estimates for
Cholesterol n=559 n=742 n=156
hyperglycemia-related adverse events in patients treated with atypical
Change from baseline 0.6 6.9 1.8
antipsychotics are not available.
Triglycerides n=183 n=307 n=123
Patients with an established diagnosis of diabetes mellitus who are started on
Change from baseline -17.4 -4.9 -8.3
atypical antipsychotics, including RISPERDAL®, should be monitored regularly
Proportion of patients With Shifts
for worsening of glucose control. Patients with risk factors for diabetes mellitus
Cholesterol 2.7% 4.3% 6.3%
(e.g., obesity, family history of diabetes) who are starting treatment with atypical
(<200 mg/dL to ≥240 mg/dL) (10/368) (22/516) (6/96)
antipsychotics, including RISPERDAL®, should undergo fasting blood glucose
Triglycerides 1.1% 2.7% 2.5%
testing at the beginning of treatment and periodically during treatment. Any
(<500 mg/dL to ≥500 mg/dL) (2/180) (8/301) (3/121)
patient treated with atypical antipsychotics, including RISPERDAL®, should be In
longer-term, controlled and uncontrolled studies, RISPERDAL® was
monitored for symptoms of hyperglycemia including polydipsia, polyuria,
associated with a mean change in (a) non-fasting cholesterol of +4.4 mg/dL at
polyphagia, and weakness. Patients who develop symptoms of hyperglycemia Week
24 (n=231) and +5.5 mg/dL at Week 48 (n=86); and (b) non-fasting
during treatment with atypical antipsychotics, including RISPERDAL®, should
triglycerides of +19.9 mg/dL at Week 24 (n=52).
undergo fasting blood glucose testing. In some cases, hyperglycemia has

Pooled data from 3 placebo-controlled, 3- to 6-week, fixed-dose studies in
resolved when the atypical antipsychotic, including RISPERDAL®, was
children and adolescents with schizophrenia (13-17 years of age), bipolar mania
discontinued; however, some patients required continuation of anti-diabetic (10-
17 years of age), or autistic disorder (5-17 years of age) are presented in
treatment despite discontinuation of RISPERDAL®. Table
5.
Pooled data from three double-blind, placebo-controlled schizophrenia studies Table
5. Change in Fasting Lipids from Three Placebo-Controlled, 3- to 6-Week,
and four double-blind, placebo-controlled bipolar monotherapy studies are
Fixed-Dose Studies in Children and Adolescents with Schizophrenia
presented in Table 2.
(13-17 Years of Age), Bipolar Mania (10-17 Years of Age), or Autistic
hange in Random Glucose from Seven Placebo-Controlled, 3- to 8-Week,
Table 2. C
Disorder (5 to 17 Years of Age)
Fixed- or Flexible-Dose Studies in Adult Subjects with Schizophrenia or-
RISPERDAL®
Bipolar Mania
Placebo 0.5-6 mg/day
RISPERDAL®
Mean change from baseline (mg/dL)
Placebo 1-8 mg/day >8-16 mg/day
Cholesterol n=74 n=133
Mean change from baseline (mg/dL)
Change from baseline 0.3 -0.3
n=555 n=748 n=164 LDL
n=22 n=22

Change from baseline 3.7 0.5
Serum Glucose -1.4 0.8 0.6
HDL
n=22 n=22
Proportion of patients with shifts
Change from baseline 1.6 -1.9
Serum Glucose 0.6% 0.4% 0%
Triglycerides n=77 n=138
(<140 mg/dL to ≥200 mg/dL) (3/525) (3/702) (0/158)
Change from baseline -9.0 -2.6

Proportion of patients with shifts
In longer-term, controlled and uncontrolled studies, RISPERDAL® was

Cholesterol 2.4% 3.8%
associated with a mean change in glucose of +2.8 mg/dL at Week 24 (n=151) and

(<170 mg/dL to ≥200 mg/dL) (1/42) (3/80)
+4.1 mg/dL at Week 48 (n=50).
LDL
0% 0%
Data from the placebo-controlled 3- to 6-week study in children and adolescents
(<110 mg/dL to ≥130 mg/dL) (0/16) (0/16)
with schizophrenia (13-17 years of age), bipolar mania (10-17 years of age), or HDL
0% 10%
autistic disorder (5 to 17 years of age) are presented in Table 3. (≥40
mg/dL to <40 mg/dL) (0/19) (2/20)
hange in Fasting Glucose from Three Placebo-Controlled, 3- to 6-Week,
Table 3. C
Triglycerides 1.5% 7.1%
Fixed-Dose Studies in Children and Adolescents with Schizophrenia
(<150 mg/dL to ≥200 mg/dL) (1/65) (8/113)
(13-17 years of age), Bipolar Mania (10-17 years of age), or Autistic In
longer-term, uncontrolled, open-label extension pediatric studies,
Disorder (5 to 17 years of age)-
RISPERDAL® was associated with a mean change in (a) fasting cholesterol of
RISPERDAL® +2.1
mg/dL at Week 24 (n=114); (b) fasting LDL of -0.2 mg/dL at Week 24 (n=103);
Placebo 0.5-6 mg/day (c)
fasting HDL of +0.4 mg/dL at Week 24 (n=103); and (d) fasting triglycerides of
Mean change from baseline (mg/dL) +6.8
mg/dL at Week 24 (n=120).
n=76 n=135
Weight Gain
Serum Glucose -1.3 2.6
Weight gain has been observed with atypical antipsychotic use. Clinical
Proportion of patients with shifts
monitoring of weight is recommended.
Serum Glucose 0% 0.8% Data
on mean changes in body weight and the proportion of subjects meeting a
(<100 mg/dL to ≥126 mg/dL) (0/64) (1/120)
weight gain criterion of 7% or greater of body weight from 7 placebo-controlled,
3- to
8- week, fixed- or flexible-dose studies in adult subjects with schizophrenia
In longer-term, uncontrolled, open-label extension pediatric studies, RISPERDAL® or
bipolar mania are presented in Table 6.
was associated with a mean change in fasting glucose of +5.2 mg/dL at Week 24
(n=119). Table
6. Mean Change in Body Weight (kg) and the Proportion of Subjects with

≥7% Gain in Body Weight From Seven Placebo-Controlled, 3- to
Dyslipidemia
8-Week, Fixed- or Flexible-Dose Studies in Adult Subjects With
Undesirable alterations in lipids have been observed in patients treated with
Schizophrenia or Bipolar Mania
atypical antipsychotics.

RISPERDAL®
Pooled data from 7 placebo-controlled, 3- to 8- week, fixed- or flexible-dose
Placebo 1-8 mg/day >8-16 mg/day
studies in adult subjects with schizophrenia or bipolar mania are presented in
(n=597) (n=769) (n=158)
Table 4.

Weight (kg)			
Change from baseline	-0.3	0.7	2.2
Weight Gain			
≥7% increase from baseline	2.9%	8.7%	20.9%

5

RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)
In longer-term, controlled and uncontrolled studies, RISPERDAL® was
hypotension and syncope may be minimized by limiting the initial dose to 2 mg
associated with a mean change in weight of +4.3 kg at Week 24 (n=395) and
total (either once daily or 1 mg twice daily) in normal adults and 0.5 mg twice
+5.3 kg at Week 48 (n=203).
daily in the elderly and patients with renal or hepatic impairment [see Dosage
Data on mean changes in body weight and the proportion of subjects meeting
and Administration (2.1, 2.4)]. Monitoring of orthostatic vital signs should be
the criterion of ≥7% gain in body weight from nine placebo-controlled, 3- to
considered in patients for whom this is of concern. A dose reduction should
8-week, fixed-dose studies in children and adolescents with schizophrenia be
considered if hypotension occurs. RISPERDAL® should be used with
(13-17 years of age), bipolar mania (10-17 years of age), autistic disorder
particular caution in patients with known cardiovascular disease (history of
(5-17 years of age), or other psychiatric disorders (5-17 years of age) are
myocardial infarction or ischemia, heart failure, or conduction abnormalities),
presented in Table 7.
cerebrovascular disease, and conditions which would predispose patients

to hypotension, e.g., dehydration and hypovolemia. Clinically significant
Table 7. Mean Change in Body Weight (kg) and the Proportion of Subjects With
≥7% Gain in Body Weight From Nine Placebo-Controlled, 3- to 8-Week,
hypotension has been observed with concomitant use of RISPERDAL® and
Fixed-Dose Studies in Children and Adolescents With Schizophrenia
antihypertensive medication.
(13-17 Years of Age), Bipolar Mania (10-17 Years of Age), Autistic
5.8 Leukopenia, Neutropenia, and Agranulocytosis
Disorder (5 to 17 Years of Age) or Other Psychiatric Disorders (5-17
Class Effect: In clinical trial and/or postmarketing experience, events of
Years of Age)
leukopenia/neutropenia have been reported temporally related to antipsychotic
Placebo RISPERDAL® 0.5-6 mg/day
agents, including RISPERDAL®. Agranulocytosis has also been reported.
(n=375) (n=448)
Possible risk factors for leukopenia/neutropenia include pre-existing low white
Weight (kg)
blood cell count (WBC) and history of drug-induced leukopenia/neutropenia.
Change from baseline 0.6 2.0
Patients with a history of a clinically significant low WBC or a drug-induced
Weight Gain
leukopenia/neutropenia should have their complete blood count (CBC) monitored
≥7% increase from baseline 6.9% 32.6%
frequently during the first few months of therapy and discontinuation of

-

RISPERDAL® should be considered at the first sign of a clinically significant
In longer-term, uncontrolled, open-label extension pediatric studies,
decline in WBC in the absence of other causative factors.
RISPERDAL® was associated with a mean change in weight of +5.5 kg at Week
Patients with clinically significant neutropenia should be carefully monitored for
24 (n=748) and +8.0 kg at Week 48 (n=242).
fever or other symptoms or signs of infection and treated promptly if such
In a long-term, open-label extension study in adolescent patients with
symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil
schizophrenia, weight increase was reported as a treatment-emergent adverse
count <1000/mm3) should discontinue RISPERDAL® and have their WBC followed
event in 14% of patients. In 103 adolescent patients with schizophrenia, a mean
until recovery.
increase of 9.0 kg was observed after 8 months of RISPERDAL® treatment. The
5.9 Potential for Cognitive and Motor Impairment
majority of that increase was observed within the first 6 months. The average

Somnolence was a commonly reported adverse reaction associated with
RISPERDAL® treatment, especially when ascertained by direct questioning of
patients. This adverse reaction is dose-related, and in a study utilizing a
checklist to detect adverse events, 41% of the high-dose patients (RISPERDAL®
mg/day) reported somnolence compared to 16% of placebo patients. Direct
questioning is more sensitive for detecting adverse events than spontaneous
reporting, by which 8% of RISPERDAL® 16 mg/day patients and 1% of placebo
patients reported somnolence as an adverse reaction. Since RISPERDAL® has
the potential to impair judgment, thinking, or motor skills, patients should be
cautioned about operating hazardous machinery, including automobiles, until
they are reasonably certain that RISPERDAL® therapy does not affect them
adversely.

5.10 Seizures

During premarketing testing in adult patients with schizophrenia, seizures
occurred in 0.3% (9/2607) of RISPERDAL®-treated patients, two in association
with hyponatremia. RISPERDAL® should be used cautiously in patients with a
history of seizures.

5.11 Dysphagia

Esophageal dysmotility and aspiration have been associated with antipsychotic
drug use. Aspiration pneumonia is a common cause of morbidity and mortality in
patients with advanced Alzheimer's dementia. RISPERDAL® and other
antipsychotic drugs should be used cautiously in patients at risk for aspiration
pneumonia. [see Boxed Warning and Warnings and Precautions (5.1)]

5.12 Priapism

Priapism has been reported during postmarketing surveillance. Severe priapism
may require surgical intervention.

5.13 Body Temperature Regulation

Disruption of body temperature regulation has been attributed to antipsychotic
agents. Both hyperthermia and hypothermia have been reported in association
with oral RISPERDAL® use. Caution is advised when prescribing for patients who
will be exposed to temperature extremes.

5.14 Patients with Phenylketonuria

Inform patients that RISPERDAL® M-TAB® Orally Disintegrating Tablets
contain phenylalanine. Phenylalanine is a component of aspartame. Each 4 mg
RISPERDAL® M-TAB® Orally Disintegrating Tablet contains 0.84 mg
phenylalanine; each 3 mg RISPERDAL® M-TAB® Orally Disintegrating Tablet

mice and rats [see Nonclinical Toxicology (13.1)]. Neither clinical studies nor
contains 0.63 mg phenylalanine; each 2 mg RISPERDAL® M-TAB® Orally
epidemiologic studies conducted to date have shown an association between
Disintegrating Tablet contains 0.42 mg phenylalanine; each 1 mg RISPERDAL®
chronic administration of this class of drugs and tumorigenesis in humans; the
M-TAB® Orally Disintegrating Tablet contains 0.28 mg phenylalanine; and each
available evidence is considered too limited to be conclusive at this time.
0.5 mg RISPERDAL® M-TAB® Orally Disintegrating Tablet contains 0.14 mg

phenylalanine.

5.7 Orthostatic Hypotension

6 adverse reactions

RISPERDAL® may induce orthostatic hypotension associated with dizziness,
tachycardia, and in some patients, syncope, especially during the initial dose-
The following are discussed in more detail in other sections of the labeling:
titration period, probably reflecting its alpha-adrenergic antagonistic properties.
• Increased mortality in elderly patients with dementia-related psychosis [see
Syncope was reported in 0.2% (6/2607) of RISPERDAL®-treated patients in
Boxed Warning and Warnings and Precautions (5.1)]
Phase 2 and 3 studies in adults with schizophrenia. The risk of orthostatic
• Cerebrovascular adverse events, including stroke, in elderly patients with

dementia-related psychosis [see Warnings and Precautions (5.2)]

6

RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)
• Neuroleptic malignant syndrome [see Warnings and Precautions (5.3)]
Table 8. Adverse Reactions in ≥2% of RISPERDAL®-Treated Adult Patients (and
• Tardive dyskinesia [see Warnings and Precautions (5.4)]
greater than placebo) with Schizophrenia in Double-Blind, Placebo-
• Metabolic Changes (Hyperglycemia and diabetes mellitus, Dyslipidemia, and
Controlled Trials (continued)
Weight Gain) [see Warnings and Precautions (5.5)]
Percentage of Patients
• Hyperprolactinemia [see Warnings and Precautions (5.6)]
Reporting Reaction
• Orthostatic hypotension [see Warnings and Precautions (5.7)]-
RISPERDAL®
• Leukopenia, neutropenia, and agranulocytosis [see Warnings and Precautions
2-8 mg >8-16 mg
(5.8)]
System/Organ Class per day per day Placebo

Adverse Reaction (N=366) (N=198) (N=225)
• Potential for cognitive and motor impairment [see Warnings and Precautions
(5.9)]
Infections and Infestations

Nasopharyngitis 3 4 3
• Seizures [see Warnings and Precautions (5.10)]

Upper
respiratory tract infection 2 3 1
• Dysphagia [see Warnings and Precautions (5.11)]
Sinusitis 1 2 1
• Priapism [see Warnings and Precautions (5.12)]
Urinary tract infection 1 3 0
• Disruption of body temperature regulation [see Warnings and Precautions
Investigations
(5.13)] Blood
creatine phosphokinase 1 2 <1
• Patients with Phenylketonuria [see Warnings and Precautions (5.14)].
increased
The most common adverse reactions in clinical trials (>5% and twice placebo) Heart
rate increased <1 2 0
were parkinsonism, akathisia, dystonia, tremor, sedation, dizziness, anxiety,
Musculoskeletal and Connective
blurred vision, nausea, vomiting, upper abdominal pain, stomach discomfort, Tissue
Disorders
dyspepsia, diarrhea, salivary hypersecretion, constipation, dry mouth, increased Back
pain 4 1 1
appetite, increased weight, fatigue, rash, nasal congestion, upper respiratory
Arthralgia 2 3 <1
tract infection, nasopharyngitis, and pharyngolaryngeal pain. Pain

in extremity	2	1	1
Nervous System Disorders			
Parkinsonism*	14	17	8
Akathisia*	10	10	3
Sedation	10	5	2
Dizziness	7	4	2
Dystonia*	3	4	2
Tremor*	2	3	1
Dizziness postural	2	0	0
Psychiatric Disorders			
Insomnia	32	25	27
Anxiety	16	11	11
Respiratory, Thoracic and Mediastinal Disorders			
Nasal congestion	4	6	2
Dyspnea	1	2	0
Epistaxis	<1	2	0
Skin and Subcutaneous Tissue Disorders			
Rash	1	4	1
Dry skin	1	3	0
Vascular Disorders			
Orthostatic hypotension	2	1	0

* Parkinsonism includes extrapyramidal disorder, musculoskeletal stiffness, parkinsonism, cogwheel rigidity, akinesia, bradykinesia, hypokinesia, masked facies, muscle rigidity, and Parkinson's disease. Akathisia includes akathisia and restlessness. Dystonia includes dystonia, muscle spasms, muscle contractions involuntary, muscle contracture, oculogyration, tongue paralysis. Tremor includes tremor and parkinsonian rest tremor.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Commonly-Observed Adverse Reactions in Double-Blind, Placebo-Controlled Clinical Trials – Schizophrenia

Adult Patients with Schizophrenia

Table 8 lists the adverse reactions reported in 2% or more of RISPERDAL®-treated adult patients with schizophrenia in three 4- to 8-week, double-blind, placebo-controlled trials.

Pediatric Patients with Schizophrenia

Table 8. Adverse Reactions in ≥2% of RISPERDAL®-Treated Adult Patients (and greater than placebo) with Schizophrenia in Double-Blind, Placebo-Controlled Trials

Table 9 lists the adverse reactions reported in 5% or more of RISPERDAL®-treated pediatric patients with schizophrenia in a 6-week double-blind, placebo-controlled trial.

Table 9. Adverse Reactions in ≥5% of RISPERDAL®-Treated Pediatric Patients

	Percentage of Patients Reporting Reaction		

RISPERDAL®
(and greater than placebo) with Schizophrenia in a Double-Blind Trial

Percentage of Patients Reporting Reaction System/Organ Class RISPERDAL® Adverse Reaction	2-8 mg per day (N=366)	>8-16 mg per day (N=198)	Placebo- (N=225)
System/Organ Class Cardiac Disorders Adverse Reaction	1-3 mg per day (N=55)	4-6 mg per day (N=51)	Placebo (N=54)
Tachycardia Gastrointestinal Disorders Eye Disorders	1	3	0
Salivary hypersecretion	0	10	2
Vision blurred System Disorders Gastrointestinal Disorders	3	1	1 Nervous
Sedation	24	12	4
Nausea	9	4	4
Parkinsonism*	16	28	11
Constipation	8	9	6 Tremor
11	10	6	
Dyspepsia	8	6	5
Akathisia*	9	10	4
Dry mouth	4	0	1
Dizziness	7	14	2
Abdominal discomfort	3	1	1
Dystonia*	2	6	0
Salivary hypersecretion Psychiatric Disorders	2	1	<1
Diarrhea	2	1	1
Anxiety	7	6	0
General Disorders			*

Parkinsonism includes extrapyramidal disorder, muscle rigidity, musculoskeletal
Fatigue 3 1 0
stiffness, and hypokinesia. Akathisia includes akathisia and restlessness.
Chest pain 2 2 1
Dystonia includes dystonia and oculogyration.
Asthenia 2 1 <1

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RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)
Commonly-Observed Adverse Reactions in Double-Blind, Placebo-Controlled
Pediatric Patients with Bipolar Mania
Clinical Trials — Bipolar Mania Table
12 lists the adverse reactions reported in 5% or more of RISPERDAL®-
Adult Patients with Bipolar Mania
treated pediatric patients with bipolar mania in a 3-week double-blind, placebo-
Table 10 lists the adverse reactions reported in 2% or more of RISPERDAL®-
controlled trial.
treated adult patients with bipolar mania in four 3-week, double-blind, placebo- Table
12. Adverse Reactions in ≥5% of RISPERDAL®-Treated Pediatric Patients
controlled monotherapy trials.
(and greater than placebo) with Bipolar Mania in Double-Blind,
Table 10. Adverse Reactions in ≥2% of RISPERDAL®-Treated Adult Patients (and
Placebo-Controlled Trials
greater than placebo) with Bipolar Mania in Double-Blind, Placebo-
Percentage of Patients Reporting Reaction
Controlled Monotherapy Trials-
RISPERDAL ®

0.5-2.5 mg Percentage of Patients Reporting Reaction System/Organ Class RISPERDAL® Adverse Reaction	3-6 mg per day (N=50)	Placebo (N=61)	(N=58)
System/Organ Class Adverse Reaction	1-6 mg per day (N=448)	Placebo (N=424)	Eye
Disorders			
Vision blurred Eye Disorders Gastrointestinal Disorders	4	7	0

Vision blurred	2	1	
Abdominal pain upper	16	13	5
Gastrointestinal Disorders			
Nausea	16	13	7
Nausea	5	2	
Vomiting	10	10	5
Diarrhea	3	2	
Diarrhea	8	7	2
Salivary hypersecretion	3	1	
Dyspepsia	10	3	2
Stomach discomfort	2	<1	
Stomach discomfort	6	0	2
General Disorders			
General Disorders			
Fatigue	2	1	
Fatigue	18	30	3
Nervous System Disorders			
Metabolism and Nutrition			
Parkinsonism*	25	9	
Disorders			
Sedation	11	4	
Increased appetite	4	7	2
Akathisia*	9	3	
Nervous System Disorders			
Tremor*	6	3	
Sedation	42	56	19
Dizziness	6	5	
Dizziness	16	13	5
Dystonia*	5	1	
Parkinsonism*	6	12	3
Lethargy	2	1	
Dystonia*	6	5	0
* Parkinsonism includes extrapyramidal disorder, parkinsonism, musculoskeletal			
Akathisia*	0	8	2
stiffness, hypokinesia, muscle rigidity, muscle tightness, bradykinesia, cogwheel			
Psychiatric Disorders			
rigidity. Akathisia includes akathisia and restlessness. Tremor includes tremor			
Anxiety	0	8	3
and parkinsonian rest tremor. Dystonia includes dystonia, muscle spasms,			
Respiratory, Thoracic and			
oculogyration, torticollis.			
Mediastinal Disorders			
Table 11 lists the adverse reactions reported in 2% or more of RISPERDAL®-			
Pharyngolaryngeal pain	10	3	5
treated adult patients with bipolar mania in two 3-week, double-blind, placebo-			Skin
and Subcutaneous Tissue			
controlled adjuvant therapy trials.			
Disorders			
			Rash
0	7	2	

Table 11. A dverse Reactions in ≥2% of RISPERDAL®-Treated Adult Patients (and * Parkinsonism includes musculoskeletal stiffness, extrapyramidal disorder, greater than placebo) with Bipolar Mania in Double-Blind, Placebo- bradykinesia, and nuchal rigidity. Dystonia includes dystonia, laryngospasm, and Controlled Adjunctive Therapy Trials muscle spasms. Akathisia includes restlessness and akathisia.

	Percentage of Patients Reporting Reaction	
Commonly-Observed Adverse Reactions in Double-Blind, Placebo-Controlled	RISPERDAL® +	Placebo +
Clinical Trials - Autistic Disorder		
System/Organ Class	Mood Stabilizer	Mood Stabilizer
Adverse Reaction	(N=127)	(N=126)
Cardiac Disorders		
Palpitations	2	0
Gastrointestinal Disorders		
Dyspepsia	9	8
Nausea	6	4
Diarrhea	6	4

Table 13 lists the adverse reactions reported in 5% or more of RISPERDAL®-treated pediatric patients treated for irritability associated with autistic disorder in two 8-week, double-blind, placebo-controlled trials and one 6-week double-blind, placebo-controlled study.

Table 13. Adverse Reactions in ≥5% of RISPERDAL®-Treated Pediatric Patients (and greater than placebo) Treated for Irritability Associated with

Autistic Disorder in Double-Blind, Placebo-Controlled Trials

Salivary hypersecretion	2	0

Percentage of Patients Reporting Reaction

General Disorders-		
RISPERDAL®		
Chest pain	2	1
System/Organ Class	0.5-4.0 mg/day	Placebo
Infections and Infestations		
Adverse Reaction	(N=107)	(N=115)
Urinary tract infection	2	1
Gastrointestinal Disorders		
Nervous System Disorders		
Vomiting	20	17
Parkinsonism*	14	4
Constipation	17	6
Sedation	9	4
Dry mouth	10	4
Akathisia*	8	0
Nausea	8	5
Dizziness	7	2
Salivary hypersecretion	7	1
Tremor	6	2
General Disorders and		
Lethargy	2	1
Administration Site Conditions		
Psychiatric Disorders		
Fatigue	31	9
Anxiety	3	2
Pyrexia	16	13
Respiratory, Thoracic and		
Thirst	7	4
Mediastinal Disorders		
Infections and Infestations		
Pharyngolaryngeal pain	5	2
Nasopharyngitis	19	9
Cough	2	0
Rhinitis	9	7

* Parkinsonism includes extrapyramidal disorder, hypokinesia and bradykinesia.

Upper respiratory tract infection	8	3

Akathisia includes hyperkinesia and akathisia.

Investigations		
Weight increased	8	2
Metabolism and Nutrition		
Disorders		
Increased appetite	44	15

RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)

Table 13. Adverse Reactions in ≥5% of RISPERDAL®-Treated Pediatric Patients with Autistic Disorder in Double-Blind, Placebo-Controlled Trials (continued)

Percentage of Patients Reporting Reaction

	RISPERDAL®	
System/Organ Class	0.5-4.0 mg/day	Placebo
Adverse Reaction	(N=107)	(N=115)
Nervous System Disorders		
Sedation	63	15

Drooling	12	4	

lesion, pruritus, skin disorder, rash erythematous, rash papular, rash generalized,

Headache	12	10	rash

maculopapular, acne, hyperkeratosis, seborrheic dermatitis

Tremor	8	1	
Dizziness	8	2	

Vascular Disorders: hypotension, flushing

Parkinsonism*	8	1	

Additional Adverse Reactions Reported with RISPERDAL® CONSTA®

Renal and Urinary Disorders The

following is a list of additional adverse reactions that have been reported

Enuresis	16	10	during

the premarketing evaluation of RISPERDAL® CONSTA®, regardless of

Respiratory, Thoracic and

frequency of occurrence:

Mediastinal Disorders

Cardiac Disorders: bradycardia

Cough	17	12	
Rhinorrhea	12	10	Ear

and Labyrinth Disorders: vertigo

Nasal congestion	10	4	Eye

Disorders: blepharospasm

Skin and Subcutaneous Tissue

Gastrointestinal Disorders: toothache, tongue spasm

Disorders

General Disorders and Administration Site Conditions: pain

Rash	8	5	

Infections and Infestations: lower respiratory tract infection, infection,

* Parkinsonism includes musculoskeletal stiffness, extrapyramidal disorder,

gastroenteritis, subcutaneous abscess

muscle rigidity, cogwheel rigidity, and muscle tightness.

Injury

and Poisoning: fall

Other Adverse Reactions Observed During the Clinical Trial Evaluation of

Investigations: weight decreased, gamma-glutamyltransferase increased,

Risperidone

hepatic enzyme increased

The following additional adverse reactions occurred across all placebo-

Musculoskeletal, Connective Tissue, and Bone Disorders: buttock pain

controlled, active-controlled, and open-label studies of RISPERDAL® in adults

and pediatric patients.

Nervous System Disorders: convulsion, paresthesia

Blood and Lymphatic System Disorders: anemia, granulocytopenia, neutropenia

Psychiatric Disorders: depression

Cardiac Disorders: sinus bradycardia, sinus tachycardia, atrioventricular block Skin

and Subcutaneous Tissue Disorders: eczema

first degree, bundle branch block left, bundle branch block right, atrioventricular

Vascular Disorders: hypertension

block

Discontinuations Due to Adverse Reactions

Ear and Labyrinth Disorders: ear pain, tinnitus

Schizophrenia - Adults

Endocrine Disorders: hyperprolactinemia

Approximately 7% (39/564) of RISPERDAL®-treated patients in double-blind,

Eye Disorders: ocular hyperemia, eye discharge, conjunctivitis, eye rolling, eyelid

placebo-controlled trials discontinued treatment due to an adverse reaction,

edema, eye swelling, eyelid margin crusting, dry eye, lacrimation increased,

compared with 4% (10/225) who were receiving placebo. The adverse reactions

photophobia, glaucoma, visual acuity reduced

associated with discontinuation in 2 or more RISPERDAL®-treated patients were:

Gastrointestinal Disorders: dysphagia, fecaloma, fecal incontinence, gastritis, lip Table

14. Adverse Reactions Associated With Discontinuation in 2 or More

swelling, cheilitis, aptyalism-

RISPERDAL®-Treated Adult Patients in Schizophrenia Trials

General Disorders: edema peripheral, thirst, gait disturbance, influenza-like-

RISPERDAL®

illness, pitting edema, edema, chills, sluggishness, malaise, chest discomfort,

2-8 mg/day >8-16 mg/day Placebo

face edema, discomfort, generalized edema, drug withdrawal syndrome,

Adverse Reaction	(N=366)	(N=198)	(N=225)

peripheral coldness, feeling abnormal
Dizziness 1.4% 1.0% 0%
Immune System Disorders: drug hypersensitivity
Nausea 1.4% 0% 0%
Infections and Infestations: pneumonia, influenza, ear infection, viral infection,
Vomiting 0.8% 0% 0%
pharyngitis, tonsillitis, bronchitis, eye infection, localized infection, cystitis,
Parkinsonism 0.8% 0% 0%
cellulitis, otitis media, onychomycosis, acarodermatitis, bronchopneumonia,
Somnolence 0.8% 0% 0%
respiratory tract infection, tracheobronchitis, otitis media chronic
Dystonia 0.5% 0% 0%
Investigations: body temperature increased, blood prolactin increased, alanine
Agitation 0.5% 0% 0%
aminotransferase increased, electrocardiogram abnormal, eosinophil count
Abdominal pain 0.5% 0% 0%
increased, white blood cell count decreased, blood glucose increased,

Orthostatic hypotension 0.3% 0.5% 0%
hemoglobin decreased, hematocrit decreased, body temperature decreased,

Akathisia 0.3% 2.0% 0%
blood pressure decreased, transaminases increased
Metabolism and Nutrition Disorders: decreased appetite, polydipsia, anorexia
Discontinuation for extrapyramidal symptoms (including Parkinsonism, akathisia,
Musculoskeletal and Connective Tissue Disorders: joint stiffness, joint swelling,
dystonia, and tardive dyskinesia) was 1% in placebo-treated patients, and 3.4%
musculoskeletal chest pain, posture abnormal, myalgia, neck pain, muscular in
active control-treated patients in a double-blind, placebo- and active-
weakness, rhabdomyolysis
controlled trial.
Nervous System Disorders: balance disorder, disturbance in attention,
Schizophrenia - Pediatrics
dysarthria, unresponsive to stimuli, depressed level of consciousness, movement
Approximately 7% (7/106), of RISPERDAL®-treated patients discontinued
disorder, transient ischemic attack, coordination abnormal, cerebrovascular
treatment due to an adverse reaction in a double-blind, placebo-controlled trial,
accident, speech disorder, syncope, loss of consciousness, hypoesthesia,
compared with 4% (2/54) placebo-treated patients. The adverse reactions
tardive dyskinesia, dyskinesia, cerebral ischemia, cerebrovascular disorder,
associated with discontinuation for at least one RISPERDAL®-treated patient
neuroleptic malignant syndrome, diabetic coma, head titubation were
dizziness (2%), somnolence (1%), sedation (1%), lethargy (1%), anxiety (1%),
Psychiatric Disorders: agitation, blunted affect, confusional state, middle
balance disorder (1%), hypotension (1%), and palpitation (1%).
insomnia, nervousness, sleep disorder, listlessness, libido decreased, and
anorgasmia

9

RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)
Bipolar Mania - Adults
Changes in ECG Parameters
In double-blind, placebo-controlled trials with RISPERDAL® as monotherapy,
Between-group comparisons for pooled placebo-controlled trials in adults
approximately 6% (25/448) of RISPERDAL®-treated patients discontinued
revealed no statistically significant differences between risperidone and placebo
treatment due to an adverse event, compared with approximately 5% (19/424) of in
mean changes from baseline in ECG parameters, including QT, QTc, and PR
placebo-treated patients. The adverse reactions associated with discontinuation
intervals, and heart rate. When all RISPERDAL® doses were pooled from
in RISPERDAL®-treated patients were:
randomized controlled trials in several indications, there was a mean increase in

heart rate of 1 beat per minute compared to no change for placebo patients. In
Table 15. Adverse Reactions Associated With Discontinuation in 2 or More
short-term schizophrenia trials, higher doses of risperidone (8-16 mg/day) were
RISPERDAL®-Treated Adult Patients in Bipolar Mania Clinical Trials
associated with a higher mean increase in heart rate compared to placebo
RISPERDAL® (4-6
beats per minute). In pooled placebo-controlled acute mania trials in adults,

	1-6 mg/day (N=448)	Placebo (N=424)
Adverse Reaction		
Parkinsonism	0.4%	0%
Lethargy	0.2%	0%
Dizziness	0.2%	0%
Alanine aminotransferase increased	0.2%	0.2%
Aspartate aminotransferase increased	0.2%	0.2%

there were small decreases in mean heart rate, similar among all treatment groups.

In the two placebo-controlled trials in children and adolescents with autistic disorder (aged 5 - 16 years) mean changes in heart rate were an increase of 8.4 beats per minute in the RISPERDAL® groups and 6.5 beats per minute in the placebo group. There were no other notable ECG changes.

In a placebo-controlled acute mania trial in children and adolescents (aged 10 — 17 years), there were no significant changes in ECG parameters, other than the increased effect of R

ISPERDAL® to transiently increase pulse rate (< 6 beats per minute). In two controlled schizophrenia trials in adolescents (aged 13 — 17 years), there were no clinically meaningful changes in ECG parameters including corrected QT intervals between treatment groups or within treatment groups over time.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of risperidone. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These adverse reactions include: alopecia, anaphylactic reaction, angioedema, atrial fibrillation, cardiopulmonary arrest, diabetic ketoacidosis in patients with impaired glucose metabolism, dysgeusia, hypoglycemia, hypothermia, ileus, inappropriate antidiuretic hormone secretion, intestinal obstruction, jaundice, mania, pancreatitis, pituitary adenoma, precocious puberty, pulmonary embolism, QT prolongation, sleep apnea syndrome, sudden death, thrombocytopenia, thrombotic thrombocytopenic purpura, urinary retention, and water intoxication.

7 Drug Interactions

7.1 Pharmacokinetic-related Interactions

The dose of RISPERDAL® should be adjusted when used in combination with CYP2D6 enzyme inhibitors (e.g., fluoxetine, and paroxetine) and enzyme inducers (e.g., carbamazepine) [see Table 18 and Dosage and Administration (2.5)]. Dose adjustment is not recommended for RISPERDAL® when co-administered with ranitidine, cimetidine, amitriptyline, or erythromycin [see Table 18].

Table 18 Summary of Effect of Coadministered Drugs on Exposure to Active

Table 16.

Moiety (Risperidone + 9-Hydroxy-Risperidone) in Healthy Subjects or
Dose Groups Placebo RISPERDAL® RISPERDAL® RISPERDAL® RISPERDAL®
Patients with Schizophrenia
2 mg 6 mg 10 mg 16 mg
Coadministered Drug Dosing Schedule Effect on Risperidone Dose
Parkinsonism 1.2 0.9 1.8 2.4 2.6
Active Moiety Recommendation
EPS Incidence 13% 17% 21% 21% 35%
(Risperidone

+ 9-Hydroxy-
Similar methods were used to measure extrapyramidal symptoms (EPS) in an
Risperidone
8-week trial comparing 5 fixed doses of RISPERDAL® (1, 4, 8, 12, and 16 mg/day):
(Ratio*)
Table 17.
Coadministered Risperidone AUC Cmax
Dose Groups RISPERDAL® RISPERDAL® RISPERDAL® RISPERDAL® RISPERDAL®
Drug
1 mg 4 mg 8 mg 12 mg 16 mg
Enzyme (CYP2D6)
Parkinsonism 0.6 1.7 2.4 2.9 4.1
Inhibitors
EPS Incidence 7% 12% 17% 18% 20%
Fluoxetine 20 mg/day 2 or 3 mg 1.4 1.5 Re-evaluate

twice daily dosing. Do not
Dystonia
exceed 8 mg/day
Class Effect: Symptoms of dystonia, prolonged abnormal contractions of muscle
Paroxetine 10 mg/day 4 mg/day 1.3 - Re-evaluate
groups, may occur in susceptible individuals during the first few days of
20 mg/day 4 mg/day 1.6 - dosing. Do not
treatment. Dystonic symptoms include: spasm of the neck muscles, sometimes
40 mg/day 4 mg/day 1.8 - exceed 8 mg/day
progressing to tightness of the throat, swallowing difficulty, difficulty breathing,
Enzyme (CYP3A/ PgP
and/or protrusion of the tongue. While these symptoms can occur at low doses,
inducers) Inducers
they occur more frequently and with greater severity with high potency and at
Carbamazepine 573 ± 168 mg/day 3 mg twice 0.51 0.55 Titrate dose

daily upwards. Do not
higher doses of first generation antipsychotic drugs. An elevated risk of acute

exceed twice the
dystonia is observed in males and younger age groups.
patient’s usual
Other Adverse Reactions
dose
Adverse event data elicited by a checklist for side effects from a large study
Enzyme (CYP3A)
comparing 5 fixed doses of RISPERDAL® (1, 4, 8, 12, and 16 mg/day) were
Inhibitors
explored for dose-relatedness of adverse events. A Cochran-Armitage Test for
Ranitidine 150 mg twice 1 mg single 1.2 1.4 Dose adjustment
trend in these data revealed a positive trend (p<0.05) for the following adverse
daily dose not needed
reactions: somnolence, vision abnormal, dizziness, palpitations, weight increase,
Cimetidine 400 mg twice 1 mg single 1.1 1.3 Dose adjustment

daily dose not needed
erectile dysfunction, ejaculation disorder, sexual function abnormal, fatigue, and

Erythromycin 500 mg four 1 mg single 1.1 0.94 Dose adjustment
skin discoloration.
times daily dose not needed
Changes in Body Weight
Other Drugs
Weight gain was observed in short-term, controlled trials and longer-term
Amitriptyline 50 mg twice 3 mg twice 1.2 1.1 Dose adjustment
uncontrolled studies in adult and pediatric patients [see Warnings and
daily daily not needed
Precautions (5.5), Adverse Reactions (6), and Use in Specific Populations (8.4)]. *

Change relative to reference

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RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)
Effect of Risperidone on other drugs drug-
treated dams. In addition, there was an increase in deaths by Day 1 among
Lithium pups
of drug-treated dams, regardless of whether or not the pups were
Repeated oral doses of RISPERDAL® (3 mg twice daily) did not affect the
cross-fostered. Risperidone also appeared to impair maternal behavior in that
exposure (AUC) or peak plasma concentrations (Cmax) of lithium (n=13). Dose pup
body weight gain and survival (from Day 1 to 4 of lactation) were reduced in
adjustment for lithium is not recommended. pups
born to control but reared by drug-treated dams. These effects were all
noted
at the one dose of risperidone tested, i.e., 5 mg/kg or 3 times the MRHD on
Valproate a
mg/m2 body surface area basis.
Repeated oral doses of R ISPERDAL® (4 mg once daily) did not affect the pre-
dose or average plasma concentrations and exposure (AUC) of valproate
Placental transfer of risperidone occurs in rat pups.
(1000 mg/day in three divided doses) compared to placebo (n=21). However, 8.2
Labor and Delivery
there was a 20% increase in valproate peak plasma concentration (Cmax) after The
effect of RISPERDAL® on labor and delivery in humans is unknown.
concomitant administration of RISPERDAL®. Dose adjustment for valproate is 8.3
Nursing Mothers
not recommended.

Risperidone and 9-hydroxyrisperidone are present in human breast milk.
Digoxin
Because of the potential for serious adverse reactions in nursing infants from
RISPERDAL® (0.25 mg twice daily) did not show a clinically relevant effect on the
risperidone, a decision should be made whether to discontinue nursing or
pharmacokinetics of digoxin. Dose adjustment for digoxin is not recommended. to
discontinue the drug, taking into account the importance of the drug to
7.2 Pharmacodynamic-related Interactions the
mother.
Centrally-Acting Drugs and Alcohol 8.4
Pediatric Use
Given the primary CNS effects of risperidone, caution should be used when
Approved Pediatric Indications
RISPERDAL® is taken in combination with other centrally-acting drugs and
Schizophrenia
alcohol. The
efficacy and safety of RISPERDAL® in the treatment of schizophrenia were
Drugs with Hypotensive Effects
demonstrated in 417 adolescents, aged 13 – 17 years, in two short-term (6 and
Because of its potential for inducing hypotension, RISPERDAL® may enhance the 8
weeks, respectively) double-blind controlled trials [see Indications and Usage
hypotensive effects of other therapeutic agents with this potential. (1.1),
Adverse Reactions (6.1), and Clinical Studies (14.1)]. Additional safety and

efficacy information was also assessed in one long-term (6-month) open-label
Levodopa and Dopamine Agonists
extension study in 284 of these adolescent patients with schizophrenia.
RISPERDAL® may antagonize the effects of levodopa and dopamine agonists. Safety
and effectiveness of RISPERDAL® in children less than 13 years of age
Clozapine with
schizophrenia have not been established.
Chronic administration of clozapine with RISPERDAL® may decrease the Bipolar
I Disorder
clearance of risperidone. The
efficacy and safety of RISPERDAL® in the short-term treatment of acute
8 Use in Specific Populations
manic or mixed episodes associated with Bipolar I Disorder in 169 children and
8.1 Pregnancy
adolescent patients, aged 10 – 17 years, were demonstrated in one double-blind,
Pregnancy Category C
placebo-controlled, 3-week trial [see Indications and Usage (1.2), Adverse

Reactions (6.1), and Clinical Studies (14.2)].
Risk Summary

Adequate and well controlled studies with RISPERDAL have not been conducted
and effectiveness of RISPERDAL® in children less than 10 years of age
in pregnant women. Neonates exposed to antipsychotic drugs (including
bipolar disorder have not been established.
RISPERDAL®) during the third trimester of pregnancy are at risk for
Autistic Disorder
extrapyramidal and/or withdrawal symptoms following delivery. There was no
efficacy and safety of RISPERDAL® in the treatment of irritability associated
increase in the incidence of malformations in embryo-fetal studies in rats and
autistic disorder were established in two 8-week, double-blind, placebo-
rabbits at 0.4–6 times MHRD. Increased pup mortality was noted at all doses in
controlled trials in 156 children and adolescent patients, aged 5 to 16 years [see
peri-postnatal studies in rats. RISPERDAL® should be used during pregnancy
Indications and Usage (1.3), Adverse Reactions (6.1) and Clinical Studies (14.4)].
only if the potential benefit justifies the potential risk to the fetus.
Additional safety information was also assessed in a long-term study in patients
Clinical Considerations
autistic disorder, or in short- and long-term studies in more than 1200
Fetal/Neonatal Adverse Reactions
pediatric patients with psychiatric disorders other than autistic disorder,

schizophrenia, or bipolar mania who were of similar age and weight, and who
Monitor neonates exhibiting extrapyramidal or withdrawal symptoms. Some

received similar dosages of RISPERDAL® as patients treated for irritability
neonates recover within hours or days without specific treatment; others may

associated with autistic disorder.
require prolonged hospitalization.

A
third study was a 6-week, multicenter, randomized, double-blind, placebo-
Data
controlled, fixed-dose study to evaluate the efficacy and safety of a lower than
Human Data
recommended dose of risperidone in subjects 5 to 17 years of age with autistic
There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence,
disorder and associated irritability, and related behavioral symptoms. There were
respiratory distress, and feeding disorder in neonates following in utero
weight-based, fixed doses of risperidone (high-dose and low-dose). The high
exposure to antipsychotics in the third trimester. These complications have
was 1.25 mg per day for patients weighing 20 to < 45 kg, and it was 1.75 mg
varied in severity; while in some cases symptoms have been self-limited, in other
day for patients weighing > 45 kg. The low dose was 0.125 mg per day for
cases neonates have required intensive care unit support and prolonged
patients for patients weighing 20 to < 45 kg, and it was 0.175 mg per day for
hospitalization.
patients weighing > 45 kg. The study demonstrated the efficacy of high-dose
There was one report of a case of agenesis of the corpus callosum in an infant
risperidone, but it did not demonstrate efficacy for low-dose risperidone.
exposed to risperidone in utero. The causal relationship to RISPERDAL® therapy
Adverse Reactions in Pediatric Patients
is unknown.
Tardive Dyskinesia
Animal Data
In clinical trials in 1885 children and adolescents treated with RISPERDAL®,
The teratogenic potential of risperidone was studied in three Segment II studies
2 (0.1%) patients were reported to have tardive dyskinesia, which resolved on
in Sprague-Dawley and Wistar rats (0.63-10 mg/kg or 0.4 to 6 times the maximum
discontinuation of RISPERDAL® treatment [see also Warnings and Precautions
recommended human dose [MRHD] on a mg/m2 body surface area basis) and in
(5.4)].
one Segment II study in New Zealand rabbits (0.31-5 mg/kg or 0.4 to 6 times the

Weight
Gain
MRHD on a mg/m2 body surface area basis). There were no teratogenic effects
in offspring of rats or rabbits given 0.4 to 6 times the MRHD on a mg/m2 body
Weight gain has been observed in children and adolescents during treatment
surface area basis. In three reproductive studies in rats (two Segment III and a
with-RISPERDAL®. Clinical monitoring of weight is recommended during
multigenerational study), there was an increase in pup deaths during the first
treatment.
4 days of lactation at doses of 0.16-5 mg/kg or 0.1 to 3 times the MRHD on a
Data derive from short-term placebo-controlled trials and longer-term
mg/m2 body surface area basis. It is not known whether these deaths were due

uncontrolled studies in pediatric patients (ages 5 to 17 years) with schizophrenia, bipolar disorder, autistic disorder, or other psychiatric disorders. In the short-term trials (3 to 8 weeks), the mean weight gain for RISPERDAL®-treated patients was 2 kg, compared to 0.6 kg for placebo-treated patients. In these trials, approximately 33% of the RISPERDAL® group had weight gain >7%, compared to 7% in the placebo group. In longer-term, uncontrolled, open-label pediatric studies, the mean weight gain was 5.5 kg at Week 24 and 8 kg at Week 48 [see Warnings and Precautions (5.5) and Adverse Reactions (6.1)].

There was no no-effect dose for increased rat pup mortality. In one Segment III study, there was an increase in stillborn rat pups at a dose of 2.5 mg/kg or 1.5 times the MRHD on a mg/m2 body surface area basis. In a cross-fostering study in Wistar rats, toxic effects on the fetus or pups were observed, as evidenced by a decrease in the number of live pups and an increase in the number of dead pups at birth (Day 0), and a decrease in birth weight in pups of

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RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)
Somnolence 8.7
Hepatic Impairment
Somnolence was frequently observed in placebo-controlled clinical trials of
While the pharmacokinetics of risperidone in subjects with liver disease were
pediatric patients with autistic disorder. Most cases were mild or moderate in
comparable to those in young healthy subjects, the mean free fraction of
severity. These events were most often of early onset with peak incidence
risperidone in plasma was increased by about 35% because of the diminished
occurring during the first two weeks of treatment, and transient with a median
concentration of both albumin and a1-acid glycoprotein. RISPERDAL® doses should
duration of 16 days. Somnolence was the most commonly observed adverse be
reduced in patients with liver disease [see Dosage and Administration (2.4)].
reaction in the clinical trial of bipolar disorder in children and adolescents, as
8.8
Patients with Parkinson’s Disease or Lewy Body Dementia
well as in the schizophrenia trials in adolescents. As was seen in the autistic
disorder trials, these adverse reactions were most often of early onset and
Patients with Parkinson’s Disease or Dementia with Lewy Bodies can experience
transient in duration [see Adverse Reactions (6.1 and 6.2)]. Patients experiencing
increased sensitivity to RISPERDAL®. Manifestations can include confusion,
persistent somnolence may benefit from a change in dosing regimen [see
obtundation, postural instability with frequent falls, extrapyramidal symptoms,
Dosage and Administration (2.1, 2.2, and 2.3)]. and
clinical features consistent with neuroleptic malignant syndrome.
Hyperprolactinemia 9
DRUG ABUSE AND DEPENDENCE
RISPERDAL® has been shown to elevate prolactin levels in children and 9.1
Controlled Substance
adolescents as well as in adults [see Warnings and Precautions (5.6)]. In double--
RISPERDAL® (risperidone) is not a controlled substance.
blind, placebo-controlled studies of up to 8 weeks duration in children and 9.2
Abuse
adolescents (aged 5 to 17 years) with autistic disorder or psychiatric disorders
-
RISPERDAL® has not been systematically studied in animals or humans for its
other than autistic disorder, schizophrenia, or bipolar mania, 49% of patients who
received RISPERDAL® had elevated prolactin levels compared to 2% of patients
potential for abuse. While the clinical trials did not reveal any tendency for any
who received placebo. Similarly, in placebo-controlled trials in children and
drug-seeking behavior, these observations were not systematic and it is not
adolescents (aged 10 to 17 years) with bipolar disorder, or adolescents (aged 13
possible to predict on the basis of this limited experience the extent to which a
to 17 years) with schizophrenia, 82–87% of patients who received RISPERDAL®
CNS-active drug will be misused, diverted, and/or abused once marketed.
had elevated levels of prolactin compared to 3-7% of patients on placebo.
Consequently, patients should be evaluated carefully for a history of drug abuse,
Increases were dose-dependent and generally greater in females than in males
and such patients should be observed closely for signs of RISPERDAL® misuse
across indications. or
abuse (e.g., development of tolerance, increases in dose, drug-seeking
behavior).
In clinical trials in 1885 children and adolescents, galactorrhea was reported in
0.8% of RISPERDAL®-treated patients and gynecomastia was reported in 2.3% of 9.3

Dependence
RISPERDAL®-treated patients.-
RISPERDAL® has not been systematically studied in animals or humans for its
Growth and Sexual Maturation
potential for tolerance or physical dependence.
The long-term effects of RISPERDAL® on growth and sexual maturation have not 10
OVERDOSAGE
been fully evaluated in children and adolescents. 10.1
Human Experience
Juvenile Animal Studies
Premarketing experience included eight reports of acute RISPERDAL®
Juvenile dogs were treated for 40 weeks with oral risperidone doses of 0.31, 1.25,
overdosage with estimated doses ranging from 20 to 300 mg and no fatalities. In
or 5 mg/kg/day. Decreased bone length and density were seen, with a no-effect
general, reported signs and symptoms were those resulting from an
dose of 0.31 mg/kg/day. This dose produced plasma levels (AUC) of
exaggeration of the drug's known pharmacological effects, i.e., drowsiness and
risperidone plus its active metabolite paliperidone (9-hydroxy-risperidone) which
sedation, tachycardia and hypotension, and extrapyramidal symptoms. One case,
were similar to those in children and adolescents receiving the maximum
involving an estimated overdose of 240 mg, was associated with hyponatremia,
recommended human dose (MRHD) of 6 mg/day. In addition, a delay in
hypokalemia, prolonged QT, and widened QRS. Another case, involving an
sexual maturation was seen at all doses in both males and females. The above
estimated overdose of 36 mg, was associated with a seizure.
effects showed little or no reversibility in females after a 12 week drug-free
Postmarketing experience includes reports of acute RISPERDAL® overdosage,
recovery period.
with estimated doses of up to 360 mg. In general, the most frequently reported
In a study in which juvenile rats were treated with oral risperidone from days 12
signs and symptoms are those resulting from an exaggeration of the drug's
to 50 of age, a reversible impairment of performance in a test of learning and
known pharmacological effects, i.e., drowsiness, sedation, tachycardia,
memory was seen, in females only, with a no-effect dose of 0.63 mg/kg/day. This
hypotension, and extrapyramidal symptoms. Other adverse reactions reported
dose produced plasma levels (AUC) of risperidone plus paliperidone about half
since market introduction related to RISPERDAL® overdose include prolonged
those observed in humans at the MRHD. No other consistent effects on QT
interval and convulsions. Torsade de pointes has been reported in
neurobehavioral or reproductive development were seen up to the highest
association with combined overdose of RISPERDAL® and paroxetine.
testable dose (1.25 mg/kg/day). This dose produced plasma levels (AUC) of
risperidone plus paliperidone which were about two thirds of those observed in 10.2
Management of Overdosage
humans at the MRHD. For
the most up to date information on the management of RISPERDAL®

overdosage, contact a certified poison control center (1-800-222-1222 or www.
8.5 Geriatric Use

poison.org). Provide supportive care including close medical supervision and
Clinical studies of RISPERDAL® in the treatment of schizophrenia did not include

monitoring. Treatment should consist of general measures employed in the
sufficient numbers of patients aged 65 and over to determine whether or not they

management of overdosage with any drug. Consider the possibility of multiple
respond differently than younger patients. Other reported clinical experience has

drug overdosage. Ensure an adequate airway, oxygenation, and ventilation.
not identified differences in responses between elderly and younger patients.

Monitor cardiac rhythm and vital signs. Use supportive and symptomatic
In general, a lower starting dose is recommended for an elderly patient,
reflecting a decreased pharmacokinetic clearance in the elderly, as well as a
measures. There is no specific antidote to RISPERDAL®.
greater frequency of decreased hepatic, renal, or cardiac function, and of 11
DESCRIPTION
concomitant disease or other drug therapy [see Clinical Pharmacology (12.3) and-
RISPERDAL® contains risperidone, an atypical antipsychotic belonging to the
Dosage and Administration (2.4, 2.5)]. While elderly patients exhibit a greater
chemical class of benzisoxazole derivatives. The chemical designation is
tendency to orthostatic hypotension, its risk in the elderly may be minimized by 3-
[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-

limiting the initial dose to 0.5 mg twice daily followed by careful titration [see Warnings and Precautions (5.7)]. Monitoring of orthostatic vital signs should be considered in patients for whom this is of concern.

This drug is substantially excreted by the kidneys, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function [see Dosage and Administration (2.4)].

8.6 Renal Impairment

In patients with moderate to severe (Clcr 59 to 15 mL/min) renal disease, clearance of the sum of risperidone and its active metabolite decreased by 60%, compared to young healthy subjects. RISPERDAL® doses should be reduced in patients with renal disease [see Dosage and Administration (2.4)].

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RISPERDAL® (risperidone)-

RISPERDAL® (risperidone)

RISPERDAL® Tablets are for oral administration and available in 0.25 mg (dark yellow), 0.5 mg (red-brown), 1 mg (white), 2 mg (orange), 3 mg (yellow), and 4 mg (green) strengths. RISPERDAL® tablets contain the following inactive ingredients: colloidal silicon dioxide, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol, sodium lauryl sulfate, and starch (corn). The 0.25 mg, 0.5 mg, 2 mg, 3 mg, and 4 mg tablets also contain talc and titanium dioxide. The 0.25 mg tablets contain yellow iron oxide; the 0.5 mg tablets contain red iron oxide; the 2 mg tablets contain FD&C Yellow No. 6 Aluminum Lake; the 3 mg and 4 mg tablets contain D&C Yellow No. 10; the 4 mg tablets contain FD&C Blue No. 2 Aluminum Lake.

RISPERDAL® is also available as a 1 mg/mL oral solution. RISPERDAL® Oral Solution contains the following inactive ingredients: tartaric acid, benzoic acid, sodium hydroxide, and purified water.

RISPERDAL® M-TAB® Orally Disintegrating Tablets are available in 0.5 mg (light coral), 1 mg (light coral), 2 mg (coral), 3 mg (coral), and 4 mg (coral) strengths. RISPERDAL® M-TAB® Orally Disintegrating Tablets contain the following inactive ingredients: Amberlite® resin, gelatin, mannitol, glycine, simethicone, carbomer, sodium hydroxide, aspartame, red ferric oxide, and peppermint oil. In addition, the 2 mg, 3 mg, and 4 mg RISPERDAL® M-TAB® Orally Disintegrating Tablets contain xanthan gum.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of RISPERDAL®, in schizophrenia, is unknown. However, it has been proposed that the drug's therapeutic activity in schizophrenia could be mediated through a combination of dopamine Type 2 (D2)

of risperidone to the enzyme suggests this is unlikely [see Drug Interactions (7)].
and serotonin Type 2 (5HT2) receptor antagonism. The clinical effect from
In vitro studies indicate that risperidone is a relatively weak inhibitor of
RISPERDAL® results from the combined concentrations of risperidone and its
CYP 2D6. Therefore, RISPERDAL® is not expected to substantially inhibit the
major metabolite, 9-hydroxyrisperidone [see Clinical Pharmacology (12.3)].
clearance of drugs that are metabolized by this enzymatic pathway. In drug
Antagonism at receptors other than D2 and 5HT2 [see Clinical Pharmacology
interaction studies, RISPERDAL® did not significantly affect the pharmaco
(12.1)] may explain some of the other effects of RISPERDAL®.
kinetics of donepezil and galantamine, which are metabolized by CYP 2D6.

12.2 Pharmacodynamics

In vitro studies demonstrated that drugs metabolized by other CYP isozymes,
RISPERDAL® is a selective monoaminergic antagonist with high affinity (Ki of
including 1A1, 1A2, 2C9, 2C19, and 3A4, are only weak inhibitors of risperidone
0.12 to 7.3 nM) for the serotonin Type 2 (5HT2), dopamine Type 2 (D2), a1 and
metabolism.
a2 adrenergic, and H1 histaminergic receptors. RISPERDAL® acts as an
Excretion
antagonist at other receptors, but with lower potency. RISPERDAL® has low to
Risperidone and its metabolites are eliminated via the urine and, to a much
moderate affinity (Ki of 47 to 253 nM) for the serotonin 5HT1C, 5HT1D, and 5HT1A
lesser extent, via the feces. As illustrated by a mass balance study of a single 1
receptors, weak affinity (Ki of 620 to 800 nM) for the dopamine D1 and
mg oral dose of 14C-risperidone administered as solution to three healthy male
haloperidol-sensitive sigma site, and no affinity (when tested at concentrations
volunteers, total recovery of radioactivity at 1 week was 84%, including 70% in
>10-5 M) for cholinergic muscarinic or b1 and b2 adrenergic receptors.
the urine and 14% in the feces.

12.3 Pharmacokinetics

The apparent half-life of risperidone was 3 hours (CV=30%) in extensive
Absorption
metabolizers and 20 hours (CV=40%) in poor metabolizers. The apparent half-life
Risperidone is well absorbed. The absolute oral bioavailability of risperidone is
of 9-hydroxyrisperidone was about 21 hours (CV=20%) in extensive metabolizers
70% (CV=25%). The relative oral bioavailability of risperidone from a tablet is
and 30 hours (CV=25%) in poor metabolizers. The pharmacokinetics of
94% (CV=10%) when compared to a solution.
risperidone and 9-hydroxyrisperidone combined, after single and multiple doses,
Pharmacokinetic studies showed that RISPERDAL® M-TAB® Orally Disintegrating
were similar in extensive and poor metabolizers, with an overall mean
Tablets and RISPERDAL® Oral Solution are bioequivalent to RISPERDAL® Tablets.
elimination half-life of about 20 hours.
Plasma concentrations of risperidone, its major metabolite, 9-hydroxyrisperidone,
Drug-Drug Interaction Studies
and risperidone plus 9-hydroxyrisperidone are dose proportional over the dosing
[See Drug Interactions (7)].
range of 1 to 16 mg daily (0.5 to 8 mg twice daily). Following oral administration of

Specific Populations
solution or tablet, mean peak plasma concentrations of risperidone occurred at
about 1 hour. Peak concentrations of 9-hydroxyrisperidone occurred at about
Renal and Hepatic Impairment
3 hours in extensive metabolizers, and 17 hours in poor metabolizers. Steady-state
[See Use in Specific Populations (8.6 and 8.7)].
concentrations of risperidone are reached in 1 day in extensive metabolizers and
Elderly
would be expected to reach steady-state in about 5 days in poor metabolizers.
In healthy elderly subjects, renal clearance of both risperidone and
Steady-state concentrations of 9-hydroxyrisperidone are reached in 5-6 days
9-hydroxyrisperidone was decreased, and elimination half-lives were prolonged
(measured in extensive metabolizers).
compared to young healthy subjects. Dosing should be modified accordingly in
Food Effect
the elderly patients [see Use in Specific Populations (8.5)].
Food does not affect either the rate or extent of absorption of risperidone. Thus,
Pediatric
RISPERDAL® can be given with or without meals.
The pharmacokinetics of risperidone and 9-hydroxyrisperidone in children were
Distribution
similar to those in adults after correcting for the difference in body weight.
Risperidone is rapidly distributed. The volume of distribution is 1-2 L/kg. In
Race and Gender Effects
plasma, risperidone is bound to albumin and a1-acid glycoprotein. The plasma

No specific pharmacokinetic study was conducted to investigate race and protein binding of risperidone is 90%, and that of its major metabolite, gender effects, but a population pharmacokinetic analysis did not identify 9-hydroxyrisperidone, is 77%. Neither risperidone nor 9-hydroxyrisperidone important differences in the disposition of risperidone due to gender (whether displaces each other from plasma binding sites. High therapeutic concentrations corrected for body weight or not) or race.

of sulfamethazine (100 mcg/mL), warfarin (10 mcg/mL), and carbamazepine

13 NONCLINICAL TOXICOLOGY

(10mcg/mL) caused only a slight increase in the free fraction of risperidone at

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

10 ng/mL and 9-hydroxyrisperidone at 50 ng/mL, changes of unknown clinical significance.

Carcinogenesis

Carcinogenicity studies were conducted in Swiss albino mice and Wistar rats.

Metabolism

Risperidone was administered in the diet at doses of 0.63 mg/kg, 2.5 mg/kg, and Risperidone is extensively metabolized in the liver. The main metabolic pathway 10 mg/kg for 18 months to mice and for 25 months to rats. These doses are is through hydroxylation of risperidone to 9-hydroxyrisperidone by the enzyme, equivalent to approximately 2, 9, and 38 times the maximum recommended CYP 2D6. A minor metabolic pathway is through N-dealkylation. The main human dose (MRHD) for schizophrenia of 16 mg/day on a mg/kg basis or 0.2, 0.75, metabolite, 9-hydroxyrisperidone, has similar pharmacological activity as and 3 times the MRHD (mice) or 0.4, 1.5, and 6 times the MRHD (rats) on a risperidone. Consequently, the clinical effect of the drug results from the mg/m2 body surface basis. A maximum tolerated dose was not achieved in male combined concentrations of risperidone plus 9-hydroxyrisperidone.

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RISPERDAL® (risperidone)-

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mice. There were statistically significant increases in pituitary gland adenomas, Several instruments were used for assessing psychiatric signs and symptoms in endocrine pancreas adenomas, and mammary gland adenocarcinomas. The these studies, among them the Brief Psychiatric Rating Scale (BPRS), a multi- table below summarizes the multiples of the human dose on a mg/m2 (mg/kg) item inventory of general psychopathology traditionally used to evaluate the basis at which these tumors occurred.

effects of drug treatment in schizophrenia. The BPRS psychosis cluster

			Multiples of Maximum Human Dose in mg/m2 (mg/kg)		
Tumor Type	Species	Sex	Lowest Effect	Highest No-Effect	
Pituitary adenomas	mouse	female	0.75 (9.4)	0.2 (2.4)	
Endocrine pancreas adenomas	rat	male	1.5 (9.4)	0.4 (2.4)	
Mammary gland adenocarcinomas	mouse	female	0.2 (2.4)	none	
	rat	female	0.4 (2.4)	none	
	rat	male	6.0 (37.5)	1.5 (9.4)	
Mammary gland	rat	male	1.5 (9.4)	0.4 (2.4)	

(conceptual disorganization, hallucinatory behavior, suspiciousness, and unusual

thought content) is considered a particularly useful subset for assessing actively

psychotic schizophrenic patients. A second traditional assessment, the Clinical

Global Impression (CGI), reflects the impression of a skilled observer, fully familiar with the manifestations of schizophrenia, about the overall clinical state of the patient. In addition, the Positive and Negative Syndrome Scale (PANSS) and the Scale for Assessing Negative Symptoms (SANS) were employed.

The results of the trials follow:

(1) In a 6-week, placebo-controlled trial (n=160) involving titration of RISPERDAL® in doses up to 10 mg/day (twice-daily schedule), RISPERDAL® was generally superior to placebo on the BPRS total score, on the BPRS psychosis cluster, and marginally superior to placebo on the SANS.

(2) In an 8-week, placebo-controlled trial (n=513) involving 4 fixed doses of RISPERDAL® (2 mg/day, 6 mg/day, 10 mg/day, and 16 mg/day, on a twice-

daily schedule), all 4 RISPERDAL® groups were generally superior to placebo
neoplasm, Total
on the BPRS total score, BPRS psychosis cluster, and CGI severity score; the
Antipsychotic drugs have been shown to chronically elevate prolactin levels in
3 highest RISPERDAL® dose groups were generally superior to placebo on
rodents. Serum prolactin levels were not measured during the risperidone
the PANSS negative subscale. The most consistently positive responses on
carcinogenicity studies; however, measurements during subchronic toxicity
all measures were seen for the 6 mg dose group, and there was no
studies showed that risperidone elevated serum prolactin levels 5-6 fold in mice
suggestion of increased benefit from larger doses.
and rats at the same doses used in the carcinogenicity studies. An increase in (3)
In an 8-week, dose comparison trial (n=1356) involving 5 fixed doses
mammary, pituitary, and endocrine pancreas neoplasms has been found in
of RISPERDAL® (1 mg/day, 4 mg/day, 8 mg/day, 12 mg/day, and 16 mg/day, on
rodents after chronic administration of other antipsychotic drugs and is
a twice-daily schedule), the four highest RISPERDAL® dose groups were
considered to be prolactin-mediated. The relevance for human risk of the
generally superior to the 1 mg RISPERDAL® dose group on BPRS total score,
findings of prolactin-mediated endocrine tumors in rodents is unknown [see
BPRS psychosis cluster, and CGI severity score. None of the dose groups
Warnings and Precautions (5.6)].
were superior to the 1 mg group on the PANSS negative subscale. The most

consistently positive responses were seen for the 4 mg dose group.
Mutagenesis
(4)
In a 4-week, placebo-controlled dose comparison trial (n=246) involving
No evidence of mutagenic or clastogenic potential for risperidone was found in
2 fixed doses of RISPERDAL® (4 and 8 mg/day on a once-daily schedule),
the Ames gene mutation test, the mouse lymphoma assay, the in vitro rat
both RISPERDAL® dose groups were generally superior to placebo on
hepatocyte DNA-repair assay, the in vivo micronucleus test in mice, the sex-
several PANSS measures, including a response measure (>20% reduction in
linked recessive lethal test in Drosophila, or the chromosomal aberration test in
PANSS total score), PANSS total score, and the BPRS psychosis cluster
human lymphocytes or Chinese hamster ovary cells.
(derived from PANSS). The results were generally stronger for the 8 mg than
Impairment of Fertility
for the 4 mg dose group.
Risperidone (0.16 to 5 mg/kg) was shown to impair mating, but not fertility, in Long-
Term Efficacy
Wistar rats in three reproductive studies (two Segment I and a multigenerational In a
longer-term trial, 365 adult outpatients predominantly meeting DSM-IV
study) at doses 0.1 to 3 times the maximum recommended human dose (MRHD)
criteria for schizophrenia and who had been clinically stable for at least 4 weeks
on a mg/m2 body surface area basis. The effect appeared to be in females, since on an
antipsychotic medication were randomized to RISPERDAL® (2-8 mg/day) or
impaired mating behavior was not noted in the Segment I study in which males to an
active comparator, for 1 to 2 years of observation for relapse. Patients
only were treated. In a subchronic study in Beagle dogs in which risperidone
receiving RISPERDAL® experienced a significantly longer time to relapse over
was administered orally at doses of 0.31 to 5 mg/kg, sperm motility and this
time period compared to those receiving the active comparator.
concentration were decreased at doses 0.6 to 10 times the MRHD on a mg/m2
body surface area basis. Dose-related decreases were also noted in serum
Pediatrics
testosterone at the same doses. Serum testosterone and sperm parameters The
efficacy of RISPERDAL® in the treatment of schizophrenia in adolescents
partially recovered, but remained decreased after treatment was discontinued. aged
13–17 years was demonstrated in two short-term (6 and 8 weeks), double-
A no-effect dose could not be determined in either rat or dog. blind
controlled trials. All patients met DSM-IV diagnostic criteria for

schizophrenia and were experiencing an acute episode at time of enrollment. In
13.2 Animal Toxicology
the first trial (study #1), patients were randomized into one of three treatment
Juvenile dogs were treated for 40 weeks with oral risperidone doses of 0.31, 1.25,
groups: RISPERDAL® 1-3 mg/day (n = 55, mean modal dose = 2.6 mg),
or 5 mg/kg/day. Decreased bone length and density were observed with a-
RISPERDAL® 4-6 mg/day (n = 51, mean modal dose = 5.3 mg), or placebo (n = 54).
no-effect dose of 0.31 mg/kg/day. This dose produced plasma AUC levels of In
the second trial (study #2), patients were randomized to either
risperidone plus its active metabolite paliperidone (9-hydroxy-risperidone) which

RISPERDAL® 0.15-0.6 mg/day (n = 132, mean modal dose = 0.5 mg) or
were similar to those in children and adolescents receiving the maximum
RISPERDAL® 1.5–6 mg/day (n = 125, mean modal dose = 4 mg). In all cases, study
recommended human dose (MRHD) of 6 mg/day. In addition, a delay in sexual
medication was initiated at 0.5 mg/day (with the exception of the 0.15-0.6 mg/day
maturation was seen at all doses in both males and females. The above effects group
in study #2, where the initial dose was 0.05 mg/day) and titrated to the
showed little or no reversibility in females after a 12 week drug-free recovery
target dosage range by approximately Day 7. Subsequently, dosage was
period.
increased to the maximum tolerated dose within the target dose range by Day 14.
In a study in which juvenile rats were treated with oral risperidone from days 12 The
primary efficacy variable in all studies was the mean change from baseline
to 50 of age, a reversible impairment of performance in a test of learning and in
total PANSS score.
memory was observed in females only with a no-effect dose of 0.63 mg/kg/day.
Results of the studies demonstrated efficacy of RISPERDAL® in all dose groups
This dose produced plasma AUC levels of risperidone plus paliperidone about from
1-6 mg/day compared to placebo, as measured by significant reduction of
half those observed in humans at the MRHD. No other consistent effects on total
PANSS score. The efficacy on the primary parameter in the 1-3 mg/day
neurobehavioral or reproductive development were seen up to the highest group
was comparable to the 4-6 mg/day group in study #1, and similar to the
testable dose of 1.25 mg/kg/day. This dose produced plasma AUC levels of
efficacy demonstrated in the 1.5–6 mg/day group in study #2. In study #2, the
risperidone plus paliperidone which were about two thirds of those observed in
efficacy in the 1.5-6 mg/day group was statistically significantly greater than that
humans at the MRHD. in
the 0.15-0.6 mg/day group. Doses higher than 3 mg/day did not reveal any
trend
towards greater efficacy.

14 CLINICAL STUDIES

14.1 Schizophrenia

14.2 Bipolar Mania - Monotherapy

Adults

Adults

Short-Term Efficacy The
efficacy of RISPERDAL® in the treatment of acute manic or mixed episodes
The efficacy of RISPERDAL® in the treatment of schizophrenia was established was
established in two short-term (3-week) placebo-controlled trials in patients
in four short-term (4- to 8-week) controlled trials of psychotic inpatients who met who
met the DSM-IV criteria for Bipolar I Disorder with manic or mixed
DSM-III-R criteria for schizophrenia.
episodes. These trials included patients with or without psychotic features.

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The primary rating instrument used for assessing manic symptoms in these trials
The results of these trials are as follows:
was the Young Mania Rating Scale (YMRS), an 11-item clinician-rated scale
(1) In one of the 8-week, placebo-controlled trials, children and adolescents
traditionally used to assess the degree of manic symptomatology (irritability,
with autistic disorder (n=101), aged 5 to 16 years, received twice daily doses
disruptive/aggressive behavior, sleep, elevated mood, speech, increased activity,
of placebo or RISPERDAL® 0.5-3.5 mg/day on a weight-adjusted basis.
sexual interest, language/thought disorder, thought content, appearance, and-
RISPERDAL®, starting at 0.25 mg/day or 0.5 mg/day depending on baseline
insight) in a range from 0 (no manic features) to 60 (maximum score). The
weight (< 20 kg and ≥ 20 kg, respectively) and titrated to clinical response
primary outcome in these trials was change from baseline in the YMRS total
(mean modal dose of 1.9 mg/day, equivalent to 0.06 mg/kg/day), significantly
score. The results of the trials follow:
improved scores on the ABC-I subscale and on the CGI-C scale compared
(1) In one 3-week placebo-controlled trial (n=246), limited to patients with manic
with placebo.
episodes, which involved a dose range of RISPERDAL® 1-6 mg/day, once (2)
In the other 8-week, placebo-controlled trial in children with autistic disorder
daily, starting at 3 mg/day (mean modal dose was 4.1 mg/day), RISPERDAL®
(n=55), aged 5 to 12 years, RISPERDAL® 0.02 to 0.06 mg/kg/day given once or
was superior to placebo in the reduction of YMRS total score.
twice daily, starting at 0.01 mg/kg/day and titrated to clinical response (mean
(2) In another 3-week placebo-controlled trial (n=286), which involved a dose

modal dose of 0.05 mg/kg/day, equivalent to 1.4 mg/day), significantly
range of 1-6 mg/day, once daily, starting at 3 mg/day (mean modal dose was
improved scores on the ABC-I subscale compared with placebo.
5.6 mg/day), RISPERDAL® was superior to placebo in the reduction of YMRS A
third trial was a 6-week, multicenter, randomized, double-blind, placebo-
total score.
controlled, fixed-dose study to evaluate the efficacy and safety of a lower than
Pediatrics
recommended dose of risperidone in subjects (N=96) 5 to 17 years of age with
The efficacy of RISPERDAL® in the treatment of mania in children or adolescents
autistic disorder (defined by DSM-IV criteria) and associated irritability and
with Bipolar I disorder was demonstrated in a 3-week, randomized, double-blind,
related behavioral symptoms. Approximately 77% of patients were younger than
placebo-controlled, multicenter trial including patients ranging in ages from 10 to 12
years of age (mean age = 9), and 88% were male. Most patients (73%)
17 years who were experiencing a manic or mixed episode of bipolar I disorder.
weighed less than 45 kg (mean weight = 40 kg). Approximately 90% of patients
Patients were randomized into one of three treatment groups: RISPERDAL®
were antipsychotic-naïve before entering the study.
0.5-2.5 mg/day (n = 50, mean modal dose = 1.9 mg), RISPERDAL® 3-6 mg/day
There were two weight-based, fixed doses of risperidone (high-dose and low-
(n = 61, mean modal dose = 4.7 mg), or placebo (n = 58). In all cases, study
dose). The high dose was 1.25 mg per day for patients weighing 20 to < 45 kg,
medication was initiated at 0.5 mg/day and titrated to the target dosage range by
and it was 1.75 mg per day for patients weighing > 45 kg. The low dose was
Day 7, with further increases in dosage to the maximum tolerated dose within the
0.125 mg per day for patients weighing 20 to < 45 kg, and it was 0.175 mg per day
targeted dose range by Day 10. The primary rating instrument used for assessing
for patients weighing > 45 kg. The dose was administered once daily in the
efficacy in this study was the mean change from baseline in the total
morning, or in the evening if sedation occurred.
YMRS score.
The primary efficacy endpoint was the mean change in the Aberrant Behavior
Results of this study demonstrated efficacy of RISPERDAL® in both dose groups
Checklist – Irritability subscale (ABC-I) score from baseline to the end of Week 6.
compared with placebo, as measured by significant reduction of total YMRS
The study demonstrated the efficacy of high-dose risperidone, as measured by
score. The efficacy on the primary parameter in the 3-6 mg/day dose group was
the mean change in ABC-I score. It did not demonstrate efficacy for low-dose
comparable to the 0.5-2.5 mg/day dose group. Doses higher than 2.5 mg/day did
risperidone. The mean baseline ABC-I scores were 29 in the placebo group
not reveal any trend towards greater efficacy. (n
= 35), 27 in the risperidone low-dose group (n = 30), and 28 in the risperidone

high-dose group (n = 31). The mean changes in ABC-I scores were -3.5, -7.4, and
14.3 Bipolar Mania – Adjunctive Therapy with Lithium or Valproate
-12.4 in the placebo, low-dose, and high-dose group respectively. The results in
The efficacy of RISPERDAL® with concomitant lithium or valproate in the the
high-dose group were statistically significant (p< 0.001) but not in the low-
treatment of acute manic or mixed episodes was established in one controlled
dose group (p=0.164).
trial in adult patients who met the DSM-IV criteria for Bipolar I Disorder. This trial
Long-Term Efficacy
included patients with or without psychotic features and with or without a rapid-
cycling course.
Following completion of the first 8-week double-blind study, 63 patients entered
an
open-label study extension where they were treated with RISPERDAL® for
(1) In this 3-week placebo-controlled combination trial, 148 in- or outpatients on
4 or 6 months (depending on whether they received RISPERDAL® or placebo in
lithium or valproate therapy with inadequately controlled manic or mixed
the double-blind study). During this open-label treatment period, patients were
symptoms were randomized to receive RISPERDAL®, placebo, or an active
maintained on a mean modal dose of RISPERDAL® of 1.8-2.1 mg/day (equivalent
comparator, in combination with their original therapy. RISPERDAL®, in
to 0.05 - 0.07 mg/kg/day).
a dose range of 1-6 mg/day, once daily, starting at 2 mg/day (mean

Patients who maintained their positive response to RISPERDAL® (response was
modal dose of 3.8 mg/day), combined with lithium or valproate (in a

defined as ≥ 25% improvement on the ABC-I subscale and a CGI-C rating of
therapeutic range of 0.6 mEq/L to 1.4 mEq/L or 50 mcg/mL to 120 mcg/mL,

'much improved' or 'very much improved') during the 4-6 month open-label
respectively) was superior to lithium or valproate alone in the reduction of

treatment phase for about 140 days, on average, were randomized to receive
YMRS total score.-
RISPERDAL® or placebo during an 8-week, double-blind withdrawal study (n=39
(2) In a second 3-week placebo-controlled combination trial, 142 in- or
of the 63 patients). A pre-planned interim analysis of data from patients who
outpatients on lithium, valproate, or carbamazepine therapy with inadequately
completed the withdrawal study (n=32), undertaken by an independent Data
controlled manic or mixed symptoms were randomized to receive
Safety Monitoring Board, demonstrated a significantly lower relapse rate in
RISPERDAL® or placebo, in combination with their original therapy.
the RISPERDAL® group compared with the placebo group. Based on the
RISPERDAL®, in a dose range of 1-6 mg/day, once daily, starting at 2 mg/day
interim analysis results, the study was terminated due to demonstration of a
(mean modal dose of 3.7 mg/day), combined with lithium, valproate, or
statistically significant effect on relapse prevention. Relapse was defined as
carbamazepine (in therapeutic ranges of 0.6 mEq/L to 1.4 mEq/L for lithium, ≥
25% worsening on the most recent assessment of the ABC-I subscale (in
50 mcg/mL to 125 mcg/mL for valproate, or 4-12 mcg/mL for carbamazepine,
relation to baseline of the randomized withdrawal phase).
respectively) was not superior to lithium, valproate, or carbamazepine alone
in the reduction of YMRS total score. A possible explanation for the failure
16 HOW SUPPLIED/STORAGE AND HANDLING
of this trial was induction of risperidone and 9-hydroxyrisperidone clearance
16.1 How Supplied
by carbamazepine, leading to subtherapeutic levels of risperidone and-
RISPERDAL® (risperidone) Tablets
9-hydroxyrisperidone.
RISPERDAL® (risperidone) Tablets are imprinted "JANSSEN" on one side and

either "Ris 0.25", "Ris 0.5", "R1", "R2", "R3", or "R4" according to their
14.4 Irritability Associated with Autistic Disorder
respective strengths.
Short-Term Efficacy
0.25 mg dark yellow, capsule-shaped tablets: bottles of 60 NDC 50458-301-04,
The efficacy of RISPERDAL® in the treatment of irritability associated with
bottles of 500 NDC 50458-301-50, and hospital unit dose blister packs of 100
autistic disorder was established in two 8-week, placebo-controlled trials in
NDC 50458-301-01.
children and adolescents (aged 5 to 16 years) who met the DSM-IV criteria for
0.5 mg red-brown, capsule-shaped tablets: bottles of 60 NDC 50458-302-06,
autistic disorder. Over 90% of these subjects were under 12 years of age and
bottles of 500 NDC 50458-302-50, and hospital unit dose blister packs of 100
most weighed over 20 kg (16-104.3 kg).
NDC 50458-302-01.
Efficacy was evaluated using two assessment scales: the Aberrant Behavior 1
mg white, capsule-shaped tablets: bottles of 60 NDC 50458-300-06, bottles of 500
Checklist (ABC) and the Clinical Global Impression - Change (CGI-C) scale. The
NDC 50458-300-50, and hospital unit dose blister packs of 100 NDC 50458-300-01.
primary outcome measure in both trials was the change from baseline to 2
mg orange, capsule-shaped tablets: bottles of 60 NDC 50458-320-06, bottles of 500
endpoint in the Irritability subscale of the ABC (ABC-I). The ABC-I subscale
NDC 50458-320-50, and hospital unit dose blister packs of 100 NDC 50458-320-01.
measured the emotional and behavioral symptoms of autism, including 3
mg yellow, capsule-shaped tablets: bottles of 60 NDC 50458-330-06, bottles of 500
aggression towards others, deliberate self-injuriousness, temper tantrums, and
NDC 50458-330-50, and hospital unit dose blister packs of 100 NDC 50458-330-01.
quickly changing moods. The CGI-C rating at endpoint was a co-primary outcome
4
mg green, capsule-shaped tablets: bottles of 60 NDC 50458-350-06 and hospital
measure in one of the studies.

unit dose blister packs of 100 NDC 50458-350-01.

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RISPERDAL® (risperidone)-
RISPERDAL® (risperidone)
RISPERDAL® (risperidone) Oral Solution
17.8 Metabolic Changes
ISPERDAL® (risperidone) 1 mg/mL Oral Solution (NDC 50458-305-03) is supplied
R
Inform patients and caregivers that treatment with RISPERDAL® can be

in 30 mL bottles with a calibrated (in milligrams and milliliters) pipette.
associated with hyperglycemia and diabetes mellitus, dyslipidemia, and weight
The minimum calibrated volume is 0.25 mL, while the maximum calibrated volume
gain [see Warnings and Precautions (5.5)].
is 3 mL.
17.9 Tardive Dyskinesia
RISPERDAL® M-TAB® (risperidone) Orally Disintegrating Tablets
Inform patients and caregivers about the risk of tardive dyskinesia [see
RISPERDAL® M-TAB® (risperidone) Orally Disintegrating Tablets are etched on
Warnings and Precautions (5.4)].
one side with “R0.5”, “R1”, “R2”, “R3”, or “R4” according to their respective
strengths. RISPERDAL® M-TAB® Orally Disintegrating Tablets 0.5 mg, 1 mg, and
2 mg are packaged in blister packs of 4 (2 X 2) tablets. Orally Disintegrating
Tablets 3 mg and 4 mg are packaged in a child-resistant pouch containing a
RISPERDAL® Tablets
blister with 1 tablet.
Active ingredient is made in Ireland

Finished product is manufactured by:
0.5 mg light coral, round, biconvex tablets: 7 blister packages (4 tablets each) per

Janssen Ortho, LLC
box, NDC 50458-395-28, and long-term care blister packaging of 30 tablets
NDC 50458-395-30. 1 mg light coral, square, biconvex tablets: 7 blister packages
Gurabo, Puerto Rico 00778
(4 tablets each) per box, NDC 50458-315-28, and long-term care blister packaging

of 30 tablets NDC 50458-315-30.
RISPERDAL® Oral Solution

Finished product is manufactured by:
2 mg coral, square, biconvex tablets: 7 blister packages (4 tablets each) per box,

Janssen Pharmaceutica NV
NDC 50458-325-28.

Beerse, Belgium
3 mg coral, round, biconvex tablets: 28 blisters per box, NDC 50458-335-28.
4 mg coral, round, biconvex tablets: 28 blisters per box, NDC 50458-355-28.
RISPERDAL® M-TAB® Orally Disintegrating Tablets
16.2 Storage and Handling
Active ingredient is made in Ireland
RISPERDAL® Tablets should be stored at controlled room temperature
Finished product is manufactured by:
15°-25°C (59°-77°F). Protect from light and moisture.
Janssen Ortho, LLC
RISPERDAL® 1 mg/mL Oral Solution should be stored at controlled room
Gurabo, Puerto Rico 00778
temperature 15°-25°C (59°-77°F). Protect from light and freezing.

RISPERDAL® Tablets, RISPERDAL® M-TAB® Orally Disintegrating Tablets, and
RISPERDAL® M-TAB® Orally Disintegrating Tablets should be stored at
RISPERDAL® Oral Solution are manufactured for:
controlled room temperature 15°-25°C (59°-77°F).
Janssen Pharmaceuticals, Inc.
Keep out of reach of children.
Titusville, NJ 08560
17 PATIENT COUNSELING INFORMATION
Physicians are advised to discuss the following issues with patients for whom
Revised April 2014
they prescribe RISPERDAL® and their caregivers: ©
Janssen Pharmaceuticals, Inc. 2007
17.1 Orthostatic Hypotension
Advise patients and caregivers about the risk of orthostatic hypotension,
especially during the period of initial dose titration [see Warnings and
015036-140508
Precautions (5.7)].
17.2 Interference with Cognitive and Motor Performance
Inform patients and caregivers that RISPERDAL® has the potential to impair
judgment, thinking, or motor skills. Advise caution about operating hazardous
machinery, including automobiles, until patients are reasonably certain that
RISPERDAL® therapy does not affect them adversely [see Warnings and
Precautions (5.9)].
17.3 Pregnancy

Advise patients and caregivers to notify their physician if the patient becomes pregnant or intends to become pregnant during therapy [see Use in Specific Populations (8.1)].

17.4 Nursing

Inform patients and caregivers that risperidone and its active metabolite are present in human breast milk; there is a potential for serious adverse reactions from RISPERDAL® in nursing infants. Advise patients that the decision whether to discontinue nursing or to discontinue the RISPERDAL® should take into account the importance of the drug to the patient [see Use in Specific Populations (8.3)].

17.5 Concomitant Medication

Advise patients and caregivers to inform their physicians if the patient is taking, or plans to take, any prescription or over-the-counter drugs, because there is a potential for interactions [see Drug Interactions (7)].

17.6 Alcohol

Advise patients to avoid alcohol while taking RISPERDAL® [see Drug Interactions (7.2)].

17.7 Phenylketonurics

Inform patients with Phenylketonuria and caregivers that RISPERDAL® M-TAB® Orally Disintegrating Tablets contain phenylalanine. Phenylalanine is a component of aspartame. Each 4 mg RISPERDAL® M-TAB® Orally Disintegrating Tablet contains 0.84 mg phenylalanine; each 3 mg RISPERDAL® M-TAB® Orally Disintegrating Tablet contains 0.63 mg phenylalanine; each 2 mg RISPERDAL® M-TAB® Orally Disintegrating Tablet contains 0.42 mg phenylalanine; each 1 mg RISPERDAL® M-TAB® Orally Disintegrating Tablet contains 0.28 mg phenylalanine; and each 0.5 mg RISPERDAL® M-TAB® Orally Disintegrating Tablet contains 0.14 mg phenylalanine [see Warnings and Precautions (5.14)].

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Description and Clinical Pharmacology

http://www.druglib.com/druginfo/risperdal/description_pharmacology/ December 09, 2014

RISPERDAL ® (risperidone) TABLETS/ORAL SOLUTION RISPERDAL ® M-TAB ® (risperidone) ORALLY DISINTEGRATING TABLETS. DESCRIPTION. RISPERDAL ® (risperidone) is a ...

RISPERDAL®

(risperidone)

TABLETS/ORAL SOLUTION

RISPERDAL® M-TAB®

(risperidone)

ORALLY DISINTEGRATING TABLETS RISPERDAL® (risperidone) is a psychotropic agent belonging to the chemical class of benzisoxazole derivatives. The chemical designation is 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]- 6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one. Its molecular formula is C H FN O and its molecular weight is 410.49. The structural formula is: Risperidone is a white to slightly beige powder. It is practically insoluble in water, freely soluble in methylene chloride, and soluble in methanol and 0.1 HCl. RISPERDAL® tablets are available in 0.25 mg (dark yellow), 0.5 mg (red-brown), 1 mg (white), 2 mg (orange), 3 mg (yellow), and 4 mg (green) strengths. Inactive ingredients are colloidal silicon dioxide, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol, sodium lauryl sulfate, and starch (corn). Tablets of 0.25, 0.5, 2, 3, and 4 mg also contain talc and titanium dioxide. The 0.25 mg tablets contain yellow iron oxide; the 0.5 mg tablets contain red iron oxide; the 2 mg tablets contain FD&C Yellow No. 6 Aluminum Lake; the 3 mg and 4 mg tablets contain D&C Yellow No. 10; the 4 mg tablets contain FD&C Blue No. 2 Aluminum Lake. RISPERDAL® is also available as a 1 mg/mL oral solution. The inactive ingredients for this solution are tartaric acid, benzoic acid, sodium hydroxide, and purified water. RISPERDAL® M-TAB® Orally Disintegrating Tablets are available in 0.5 mg (light coral), 1 mg (light coral), 2 mg (light coral), 3 mg (coral) and 4 mg (coral) strengths. RISPERDAL® M-TAB® Orally Disintegrating Tablets contain the following inactive ingredients: Amberlite® resin, gelatin, mannitol, glycine, simethicone, carbomer,

sodium hydroxide, aspartame, red ferric oxide, and peppermint oil. In addition, the 3 mg and 4 mg RISPERDAL® M-TAB® Orally Disintegrating Tablets contain xanthan gum. The mechanism of action of RISPERDAL® (risperidone), as with other drugs used to treat schizophrenia, is unknown. However, it has been proposed that the drug's therapeutic activity in schizophrenia is mediated through a combination of dopamine Type 2 (D) and serotonin Type 2 (5HT) receptor antagonism. Antagonism at receptors other than D and 5HT may explain some of the other effects of RISPERDAL®. RISPERDAL® is a selective monoaminergic antagonist with high affinity (Ki of 0.12 to 7.3 nM) for the serotonin Type 2 (5HT), dopamine Type 2 (D),α and α adrenergic, and H histaminergic receptors. RISPERDAL® acts as an antagonist at other receptors, but with lower potency. RISPERDAL® has low to moderate affinity (Ki of 47 to 253 nM) for the serotonin 5HT , 5HT , and 5HT receptors, weak affinity (Ki of 620 to 800 nM) for the dopamine D and haloperidol-sensitive sigma site, and no affinity (when tested at concentrations >10-5 M) for cholinergic muscarinic or β and β adrenergic receptors. Risperidone is well absorbed. The absolute oral bioavailability of risperidone is 70% (CV=25%). The relative oral bioavailability of risperidone from a tablet is 94% (CV=10%) when compared to a solution. Pharmacokinetic studies showed that RISPERDAL® M-TAB® Orally Disintegrating Tablets and RISPERDAL® Oral Solution are bioequivalent to RISPERDAL® Tablets. Plasma concentrations of risperidone, its major metabolite, 9-hydroxyrisperidone, and risperidone plus 9-hydroxyrisperidone are dose proportional over the dosing range of 1 to 16 mg daily (0.5 to 8 mg BID). Following oral administration of solution or tablet, mean peak plasma concentrations of risperidone occurred at about 1 hour. Peak concentrations of 9-hydroxyrisperidone occurred at about 3 hours in extensive metabolizers, and 17 hours in poor metabolizers. Steady-state concentrations of risperidone are reached in 1 day in extensive metabolizers and would be expected to reach steady-state in about 5 days in poor metabolizers. Steady-state concentrations of 9-hydroxyrisperidone are reached in 5–6 days (measured in extensive metabolizers). Food does not affect either the rate or extent of absorption of risperidone. Thus, risperidone can be given with or without meals. Risperidone is rapidly distributed. The volume of distribution is 1–2 L/kg. In plasma, risperidone is bound to albumin and α -acid glycoprotein. The plasma protein binding of risperidone is 90%, and that of its major metabolite, 9-hydroxyrisperidone, is 77%. Neither risperidone nor 9-hydroxyrisperidone displaces each other from plasma binding sites. High therapeutic concentrations of sulfamethazine (100 mcg/mL), warfarin (10 mcg/mL), and carbamazepine (10 mcg/mL) caused only a slight increase in the free fraction of risperidone at 10 ng/mL and 9-hydroxyrisperidone at 50 ng/mL, changes of unknown clinical significance. Risperidone is extensively metabolized in the liver. The main metabolic pathway is through hydroxylation of risperidone to 9-hydroxyrisperidone by the enzyme, CYP 2D6. A minor metabolic pathway is through N-dealkylation. The main metabolite, 9-hydroxyrisperidone, has similar pharmacological activity as risperidone. Consequently, the clinical effect of the drug (e.g., the active moiety) results from the combined concentrations of risperidone plus 9-hydroxyrisperidone. CYP 2D6, also called debrisoquin hydroxylase, is the enzyme responsible for metabolism of many neuroleptics, antidepressants, antiarrhythmics, and other drugs. CYP 2D6 is subject to genetic polymorphism (about 6%–8% of Caucasians, and a very low percentage of Asians, have little or no activity and are "poor metabolizers") and to inhibition by a variety of substrates and some non-substrates, notably quinidine. Extensive CYP 2D6 metabolizers convert risperidone rapidly into 9-hydroxyrisperidone, whereas poor CYP 2D6 metabolizers convert it much more slowly. Although extensive metabolizers have lower risperidone and higher 9-hydroxyrisperidone concentrations than poor metabolizers, the pharmacokinetics of the active moiety, after single and multiple doses, are similar in extensive and poor metabolizers. Risperidone could be subject to two kinds of drug-drug interactions (see PRECAUTIONS– Drug Interactions). First, inhibitors of CYP 2D6 interfere with conversion of risperidone to 9-hydroxyrisperidone. This occurs with quinidine, giving essentially all recipients a risperidone pharmacokinetic profile typical of poor metabolizers. The therapeutic benefits and adverse effects of risperidone in patients receiving quinidine have not been evaluated, but observations in a modest number (n 70) of poor metabolizers given risperidone do not suggest important differences between poor and extensive metabolizers. Second, co-administration of known enzyme inducers (e.g., phenytoin, rifampin, and phenobarbital) with risperidone may cause a decrease in the combined plasma concentrations of risperidone and 9-hydroxyrisperidone. It would also be possible for risperidone to interfere with metabolism of other drugs metabolized by CYP 2D6. Relatively weak binding of risperidone to the enzyme suggests this is unlikely. In a drug interaction study in schizophrenic patients, 11 subjects received risperidone titrated to 6 mg/day for 3 weeks, followed by concurrent administration of carbamazepine for an additional 3 weeks. During co-administration, the plasma concentrations of risperidone and its pharmacologically active metabolite, 9-hydroxyrisperidone, were decreased by about 50%. Plasma concentrations of carbamazepine did not appear to be affected. Co-administration of other known enzyme inducers (e.g., phenytoin, rifampin, and phenobarbital) with risperidone may cause similar decreases in the combined plasma concentrations of risperidone and 9-hydroxyrisperidone, which could lead to decreased efficacy of risperidone treatment (see PRECAUTIONS– Drug Interactions and

DOSAGE AND ADMINISTRATION – Co-Administration of RISPERDAL® with Certain Other Medications). Fluoxetine (20 mg QD) and paroxetine (20 mg QD) have been shown to increase the plasma concentration of risperidone 2.5–2.8 fold and 3–9 fold respectively. Fluoxetine did not affect the plasma concentration of 9-hydroxyrisperidone. Paroxetine lowered the concentration of 9-hydroxyrisperidone by about 10% (see PRECAUTIONS –Drug Interactions and DOSAGE AND ADMINISTRATION– Co-Administration of RISPERDAL® with Certain Other Medications). Repeated oral doses of risperidone (3 mg BID) did not affect the exposure (AUC) or peak plasma concentrations (C) of lithium (n=13) (see PRECAUTIONS– Drug Interactions). Repeated oral doses of risperidone (4 mg QD) did not affect the pre-dose or average plasma concentrations and exposure (AUC) of valproate (1000 mg/day in three divided doses) compared to placebo (n=21). However, there was a 20% increase in valproate peak plasma concentration (C) after concomitant administration of risperidone (see PRECAUTIONS– Drug Interactions). There were no significant interactions between risperidone (1 mg QD) and erythromycin (500 mg QID) (see PRECAUTIONS – Drug Interactions). Cimetidine and ranitidine increased the bioavailability of risperidone by 64% and 26%, respectively. However, cimetidine did not affect the AUC of the active moiety, whereas ranitidine increased the AUC of the active moiety by 20%. Amitriptyline did not affect the pharmacokinetics of risperidone or the active moiety. In drug interaction studies, risperidone did not significantly affect the pharmacokinetics of donepezil and galantamine, which were metabolized by CYP 2D6. RISPERDAL® (0.25 mg BID) did not show a clinically relevant effect on the pharmacokinetics of digoxin. Risperidone and its metabolites are eliminated via the urine and, to a much lesser extent, via the feces. As illustrated by a mass balance study of a single 1 mg oral dose of 14C-risperidone administered as solution to three healthy male volunteers, total recovery of radioactivity at 1 week was 84%, including 70% in the urine and 14% in the feces. The apparent half-life of risperidone was 3 hours (CV=30%) in extensive metabolizers and 20 hours (CV=40%) in poor metabolizers. The apparent half-life of 9-hydroxyrisperidone was about 21 hours (CV=20%) in extensive metabolizers and 30 hours (CV=25%) in poor metabolizers. The pharmacokinetics of the active moiety, after single and multiple doses, were similar in extensive and poor metabolizers, with an overall mean elimination half-life of about 20 hours. In patients with moderate to severe renal disease, clearance of the sum of risperidone and its active metabolite decreased by 60% compared to young healthy subjects. RISPERDAL® doses should be reduced in patients with renal disease (see PRECAUTIONS and DOSAGE AND ADMINISTRATION). While the pharmacokinetics of risperidone in subjects with liver disease were comparable to those in young healthy subjects, the mean free fraction of risperidone in plasma was increased by about 35% because of the diminished concentration of both albumin and α -acid glycoprotein. RISPERDAL® doses should be reduced in patients with liver disease (see PRECAUTIONS and DOSAGE AND ADMINISTRATION). In healthy elderly subjects, renal clearance of both risperidone and 9-hydroxyrisperidone was decreased, and elimination half-lives were prolonged compared to young healthy subjects. Dosing should be modified accordingly in the elderly patients (see DOSAGE AND ADMINISTRATION). The pharmacokinetics of risperidone and 9-hydroxyrisperidone in children were similar to those in adults after correcting for the difference in body weight. No specific pharmacokinetic study was conducted to investigate race and gender effects, but a population pharmacokinetic analysis did not identify important differences in the disposition of risperidone due to gender (whether corrected for body weight or not) or race. The efficacy of RISPERDAL® in the treatment of schizophrenia was established in four short-term (4- to 8-week) controlled trials of psychotic inpatients who met DSM-III-R criteria for schizophrenia. Several instruments were used for assessing psychiatric signs and symptoms in these studies, among them the Brief Psychiatric Rating Scale (BPRS), a multi-item inventory of general psychopathology traditionally used to evaluate the effects of drug treatment in schizophrenia. The BPRS psychosis cluster (conceptual disorganization, hallucinatory behavior, suspiciousness, and unusual thought content) is considered a particularly useful subset for assessing actively psychotic schizophrenic patients. A second traditional assessment, the Clinical Global Impression (CGI), reflects the impression of a skilled observer, fully familiar with the manifestations of schizophrenia, about the overall clinical state of the patient. In addition, the Positive and Negative Syndrome Scale (PANSS) and the Scale for Assessing Negative Symptoms (SANS) were employed. The results of the trials follow: (1)In a 6-week, placebo-controlled trial (n=160) involving titration of RISPERDAL® in doses up to 10 mg/day (BID schedule), RISPERDAL® was generally superior to placebo on the BPRS total score, on the BPRS psychosis cluster, and marginally superior to placebo on the SANS. (2)In an 8-week, placebo-controlled trial (n=513) involving 4 fixed doses of RISPERDAL® (2, 6, 10, and 16 mg/day, on a BID schedule), all 4 RISPERDAL® groups were generally superior to placebo on the BPRS total score, BPRS psychosis cluster, and CGI severity score; the 3 highest RISPERDAL® dose groups were generally superior to placebo on the PANSS negative subscale. The most consistently positive responses on all measures were seen for the 6 mg dose group, and there was no suggestion of increased benefit from larger doses. (3)In an 8-week, dose comparison trial (n=1356) involving 5 fixed doses of RISPERDAL® (1, 4, 8, 12, and 16 mg/day, on a BID schedule), the four highest RISPERDAL® dose groups were generally superior to

the 1 mg RISPERDAL® dosegroup on BPRS total score, BPRS psychosis cluster, and CGI severity score. None of the dose groups were superior to the 1 mg group on the PANSS negative subscale. The most consistently positive responses were seen for the 4 mg dose group. (4)In a 4-week, placebo-controlled dose comparison trial (n=246) involving 2 fixed doses of RISPERDAL® (4 and 8 mg/day on a QD schedule), both RISPERDAL® dose groups were generally superior to placebo on several PANSS measures, including a response measure (>20% reduction in PANSS total score), PANSS total score, and the BPRS psychosis cluster (derived from PANSS). The results were generally stronger for the 8 mg than for the 4 mg dose group. In a longer-term trial, 365 adult outpatients predominantly meeting DSM-IV criteria for schizophrenia and who had been clinically stable for at least 4 weeks on an antipsychotic medication were randomized to RISPERDAL® (2–8 mg/day) or to an active comparator, for 1 to 2 years of observation for relapse. Patients receiving RISPERDAL® experienced a significantly longer time to relapse over this time period compared to those receiving the active comparator. The efficacy of RISPERDAL® in the treatment of acute manic or mixed episodes was established in 2 short-term (3-week) placebo-controlled trials in patients who met the DSM-IV criteria for Bipolar I Disorder with manic or mixed episodes. These trials included patients with or without psychotic features. The primary rating instrument used for assessing manic symptoms in these trials was the Young Mania Rating Scale (Y-MRS), an 11-item clinician-rated scale traditionally used to assess the degree of manic symptomatology (irritability, disruptive/aggressive behavior, sleep, elevated mood, speech, increased activity, sexual interest, language/thought disorder, thought content, appearance, andinsight) in a range from 0 (no manic features) to 60 (maximum score). The primary outcome in these trials was change from baseline in the Y-MRS total score. The results of the trials follow: (1)In one 3-week placebo-controlled trial (n=246), limited to patients with manic episodes, which involved a dose range of RISPERDAL® 1–6 mg/day, once daily, starting at 3 mg/day (mean modal dose was 4.1 mg/day), RISPERDAL® was superior to placebo in the reduction of Y-MRS total score. (2)In another 3-week placebo-controlled trial (n=286), which involved a dose range of 1–6 mg/day, once daily, starting at 3 mg/day (mean modal dose was 5.6 mg/day), RISPERDAL® was superior to placebo in the reduction of Y-MRS total score. The efficacy of risperidone with concomitant lithium or valproate in the treatment of acute manic or mixed episodes was established in one controlled trial in patients who met the DSM-IV criteria for Bipolar I Disorder. This trial included patients with or without psychotic features and with or without a rapid-cycling course. (1)In this 3-week placebo-controlled combination trial, 148 in- or outpatients on lithium or valproate therapy with inadequately controlled manic or mixed symptoms were randomized to receive RISPERDAL®, placebo, or an active comparator, in combination with their original therapy. RISPERDAL®, in a dose range of 1–6 mg/day, once daily, starting at 2 mg/day (mean modal dose of 3.8 mg/day), combined with lithium or valproate (in a therapeutic range of 0.6 mEq/L to 1.4 mEq/L or 50 mcg/mL to 120 mcg/mL, respectively) was superior to lithium or valproate alone in the reduction of Y-MRS total score. (2)In a second 3-week placebo-controlled combination trial, 142 in- or outpatients on lithium, valproate, or carbamazepine therapy with inadequately controlled manic or mixed symptoms were randomized to receive RISPERDAL® or placebo, in combination with their original therapy. RISPERDAL®, in a dose range of 1–6 mg/day, once daily, starting at 2 mg/day (mean modal dose of 3.7 mg/day), combined with lithium, valproate, or carbamazepine (in therapeutic ranges of 0.6 mEq/L to 1.4 mEq/L for lithium, 50 mcg/mL to 125 mcg/mL for valproate, or 4–12 mcg/mL for carbamazepine, respectively) was not superior to lithium, valproate, or carbamazepine alone in the reduction of Y-MRS total score. A possible explanation for the failure of this trial was induction of risperidone and 9-hydroxyrisperidone clearance by carbamazepine, leading to subtherapeutic levels of risperidone and 9-hydroxyrisperidone. The efficacy of RISPERDAL® in the treatment of irritability associated with autistic disorder was established in two 8-week, placebo-controlled trials in children and adolescents (aged 5 to 16 years) who met the DSM-IV criteria for autistic disorder. Over 90% of these subjects were under 12 years of age and most weighed over 20 kg (16-104.3 kg). Efficacy was evaluated using two assessment scales: the Aberrant Behavior Checklist (ABC) and the Clinical Global Impression - Change (CGI-C) scale. The primary outcome measure in both trials was the change from baseline to endpoint in the Irritability subscale of the ABC (ABC-I). The ABC-I subscale measured the emotional and behavioral symptoms of autism, including aggression towards others, deliberate self-injuriousness, temper tantrums, and quickly changing moods. The CGI-C rating at endpoint was a co-primary outcome measure in one of the studies. The results of these trials are as follows: (1) In one of the 8-week, placebo-controlled trials, children and adolescents with autistic disorder (n=101), aged 5 to 16 years, received twice daily doses of placebo or RISPERDAL® 0.5-3.5 mg/day on a weight adjusted basis. RISPERDAL®, starting at 0.25 mg/day or 0.5 mg/day depending on baseline weight (< 20 kg and ≥ 20 kg, respectively) and titrated to clinical response (mean modal dose of 1.9 mg/day, equivalent to 0.06 mg/kg/day), significantly improved scores on the ABC-I subscale and on the CGI-C scale compared with placebo. (2) In the other 8-week, placebo-controlled trial in children with autistic disorder (n=55), aged 5 to 12 years, RISPERDAL® 0.02 to 0.06 mg/kg/day given once or twice daily, starting at 0.01 mg/kg/day and titrated to clinical response (mean modal dose of 0.05 mg/kg/day,

equivalent to 1.4 mg/day), significantly improved scores on the ABC-I subscale compared with placebo. Following completion of the first 8-week double-blind study, 63 patients entered an open-label study extension where they were treated with RISPERDAL® for 4 or 6 months (depending on whether they received RISPERDAL® or placebo in the double-blind study). During this open-label treatment period, patients were maintained on a mean modal dose of RISPERDAL® of 1.8-2.1 mg/day (equivalent to 0.05 - 0.07 mg/kg/day). Patients who maintained their positive response to RISPERDAL® (response was defined as ≥25% improvement on the ABC-I subscale and a CGI-C rating of 'much improved' or 'very much improved') during the 4-6 month open-label treatment phase for about 140 days, on average, were randomized to receive RISPERDAL® or placebo during an 8 week, double-blind withdrawal study (n=39 of the 63 patients). A pre-planned interim analysis of data from patients who completed the withdrawal study (n=32), undertaken by an independent Data Safety Monitoring Board, demonstrated a significantly lower relapse rate in the RISPERDAL® group compared with the placebo group. Based on the interim analysis results, the study was terminated due to demonstration of a statistically significant effect on relapse prevention. Relapse was defined as ≥25% worsening on the most recent assessment of the ABC-I subscale (in relation to baseline of the randomized withdrawal phase).

Psychology Wiki

http://psychology.wikia.com/wiki/Risperidone December 09, 2014

Risperidone (pronounced Ris-PER-ĭ-dōn and sold under the trade name Risperdal in the Netherlands, United States, Canada, the United Kingdom, [Portugal and several ...

Risperidone (pronounced Ris-PER-ĭ-dōn and sold under the trade name Risperdal in the Netherlands, United States, Canada, the United Kingdom, [Portugal and several other countries, Risperdal or Ridal in New Zealand, Rispolept in Eastern Europe, and Belivon, or Rispen elsewhere) is an atypical antipsychotic developed by Janssen-Cilag.

Risperidone was approved by the United States Food and Drug Administration (FDA) in 1993[1] for the treatment of schizophrenia. On August 22, 2007, Risperdal was approved as the only drug agent available for treatment of schizophrenia in youth ages 13–18; it was also approved that same day for treatment of bipolar disorder in youth and children ages 10–18, joining lithium. Risperidone contains the functional groups of benzisoxazole and piperidine as part of its molecular structure. In 2003 the FDA approved risperidone for the short-term treatment of the mixed and manic states associated with bipolar disorder. In 2006 the FDA approved risperidone for the treatment of irritability in children and adolescents with autism. The FDA's decision was based in part on a study of autistic children with severe and enduring problems of tantrums, aggression, and self-injury; risperidone is not recommended for autistic children with mild aggression and explosive behavior without an enduring pattern.[2] Like other atypical antipsychotics, risperidone has also been used off-label for the treatment of anxiety disorders, such as obsessive-compulsive disorder; severe, treatment-resistant depression with or without psychotic features; Tourette syndrome; disruptive behavior disorders in children; and eating disorders, among others.[3] In two small studies risperidone was reported to successfully treat the symptoms of phencyclidine psychosis due to acute intoxication[4] and chronic use.[5]

A multi-year UK study by the Alzheimer's Research Trust suggested that this and other neuroleptic anti-psychotic drugs commonly given to Alzheimer's patients with mild behavioural problems often made their condition worse. The study concluded that:

Janssen's patent on Risperdal expired on December 29, 2007, opening the market for cheaper generic versions of the drug from other companies; however, Janssen had exclusive marketing rights until June 29, 2008, as the result of a pediatric extension.

Risperidone is available as a tablet in 0.25, 0.5, 1, 2, 3 and 4 mg sizes, as an oral solution (30ml, 1mg/ml), and as a 25 mg, 37.5 mg and 50 mg ampoule Risperdal Consta, which is a depot injection administered once every two weeks. It is also available as a wafer known in the United States as Risperdal M-Tabs and elsewhere as Risperdal Quicklets.

Risperdone became available as a generic drug in October 2008 from Teva Pharmaceuticals and Patriot Pharmaceutics. The Patriot generic is Janssen Pharmaceutical's "authorized generic pharmaceutical."

Common side effects include akathisia, anxiety, insomnia, low blood pressure, muscle stiffness, muscle pain, sedation, sexual dysfunction, tremors, increased salivation, and stuffy nose. Risperidone has been associated with minimal to moderate weight gain, with one study finding that 26 to 38 percent of

participants on the drug experienced weight gain.[7][8]

Occasionally breast tenderness and eventually lactation in both genders may occur. Many antipsychotics are known to increase prolactin because they inhibit dopamine. However, risperidone is known to increase prolactin to a greater extent than most other antipsychotics, such as quetiapine. It is thought that once risperidone raises prolactin, it may cause non-cancerous tumors in the pituitary gland. This may recur even if the patient has switched to a different antipsychotic.[9]

Risperidone can potentially cause tardive dyskinesia (TD),[10] extrapyramidal symptoms (EPS),[10] and neuroleptic malignant syndrome (NMS).[10]

Also, Risperidone can trigger diabetes and more serious conditions of glucose metabolism, including ketoacidosis and hyperosmolar coma.[11]

This drug belongs to a class of anti-psychotic drugs known as atypical neuroleptics. It is a strong dopamine antagonist. It has high affinity for D dopaminergic receptors. It has actions at several 5-HT (serotonin) receptor subtypes. These are 5-HT , linked to weight gain, 5-HT ,linked to its antipsychotic action and relief of some of the extrapyramidal side effects experienced with the typical neuroleptics through action at 5-HT . The latter action may lead to an increased release of dopamine from mesocortical neurones in the brain.

It reaches peak plasma levels quickly regardless of whether it is administered as a liquid or pill. Risperidone is metabolised fairly quickly, so this potential for nausea subsides usually in two to three hours. However, the active metabolite, 9-hydroxy-risperidone, which has similar pharmacodynamics to risperidone, lingers in the body for much longer, and has been developed as an antipsychotic in its own right, called paliperidone.

An intramuscular preparation, marketed as Risperdal Consta, can be given once every two weeks. It is slowly released from the injection site. It can be useful in patients who have difficulty taking oral medication for any reason. Some people prefer a once-every-two-weeks injection to daily pills[How to reference and link to summary or text]. It also helps the physician ensure compliance. Doses range from 25 to 50 mg given as an intramuscular injection once every two weeks.