

New Zealand Datasheet

Name of Medicine

RISPERIDONE tablets

Risperidone 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg tablets

Presentation

Risperidone oral, film-coated tablets are available in the following strengths:

0.5 mg risperidone:	Brown, capsule shaped, biconvex film-coated tablets with '0.5' on one side and 'RSP' on the other side with 'R' and 'SP' separated by a score line.
1 mg risperidone:	White, capsule shaped, biconvex film-coated tablets with '1' on one side and 'RSP' on the other side with 'R' and 'SP' separated by a score line.
2 mg risperidone:	Orange, capsule shaped, biconvex film-coated tablets with '2' on one side and 'RSP' on the other side with 'R' and 'SP' separated by a score line.
3 mg risperidone:	Yellow, capsule shaped, biconvex film-coated tablets with '3' on one side and 'RSP' on the other side with 'R' and 'SP' separated by a score line.
4 mg risperidone:	Green, capsule shaped, biconvex film-coated tablets with '4' on one side and 'RSP' on the other side with 'R' and 'SP' separated by a score line.

Uses

Actions

Risperidone is a compound, which belongs to a new class of antipsychotic agents, the benzisoxazole derivatives.

Risperidone is a selective monoaminergic antagonist having a high affinity for serotonergic 5-HT₂ and dopaminergic D₂ receptors. Risperidone binds also to alpha₁-adrenergic receptors and, with lower affinity, to H₁-histamine and alpha₂-adrenergic receptors. Risperidone has no affinity for cholinergic receptors. The antipsychotic activity of risperidone is considered to be attributable to both risperidone and its active metabolite 9-hydroxy risperidone. Risperidone, as a potent D₂ antagonist, improves the positive symptoms of schizophrenia but causes less depression of motor activity and induction of catalepsy than classical neuroleptics. Balanced central serotonin and dopamine antagonism may reduce extrapyramidal side effect liability and extend the therapeutic activity to the negative and affective symptoms of schizophrenia.

Pharmacokinetics

Risperidone is completely absorbed after oral administration, reaching peak plasma concentrations within 1 to 2 hours. The absorption is not affected by food and thus Risperidone tablets may be given with or without meals.

Risperidone is partly metabolised by CYP2D6 to 9-hydroxyrisperidone, which has similar pharmacological activity to risperidone. Another metabolic pathway is N-dealkylation.

After oral administration to psychotic patients, risperidone is eliminated with a half-life of about 3 hours. The elimination half-life of 9-hydroxy-risperidone and of risperidone plus 9-hydroxy risperidone is 24 hours.

Steady-state of risperidone is reached within 1 day in most patients. Steady-state of 9-hydroxy-risperidone is reached within 4-5 days of dosing. Risperidone plasma concentrations are dose-proportional within the therapeutic dose range.

Risperidone is rapidly distributed. The volume of distribution is 1-2 L/kg. In plasma, risperidone is bound to albumin and alpha₁-acid glycoprotein. The plasma protein binding of risperidone is 88%, while that of 9-hydroxy-risperidone is 77%.

One week after administration, 70% of the dose is excreted in the urine and 14% in the faeces. In urine, risperidone plus 9-hydroxy-risperidone represents 35-45% of the dose.

A single-dose study showed higher active plasma concentrations and a reduced clearance of risperidone plus 9-hydroxy risperidone by 30% in the elderly and 60% in patients with renal insufficiency. Risperidone plasma concentrations were normal in patients with liver insufficiency, but the unbound risperidone in plasma was increased by about 35%.

Indications

Risperidone tablets are indicated for the treatment of schizophrenia and other psychotic disorders. These include first episode psychoses, acute schizophrenic exacerbations, chronic schizophrenia and other psychotic conditions, in which positive symptoms (such as hallucinations, delusions, thought disturbances, hostility, suspiciousness), and/or negative symptoms (such as blunted affect, emotional and social withdrawal, poverty of speech) are prominent.

Risperidone tablets are also indicated for the treatment and long term control of mania in bipolar disorder. These episodes are characterised by symptoms such as elevated, expansive or irritable mood, inflated self esteem, decreased need for sleep, pressured speech, racing thoughts, distractibility, or poor judgement, including disruptive or aggressive behaviours.

Risperidone tablets also alleviate affective symptoms (such as depression, guilt-feelings, anxiety) associated with schizophrenia. In addition, Risperidone tablets also appear effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial response to treatment with this agent.

Risperidone tablets are also indicated for the treatment of behavioural and psychological symptoms of dementia such as aggressiveness (verbal outburst, physical violence), activity disturbance (agitation, wandering) or psychotic symptoms. Risperidone tablets are also indicated for the treatment of conduct and other disruptive behaviour disorders in children (over 5 years), adolescents and adults with subaverage intellectual functioning or mental retardation, or average IQ in whom destructive behaviours (e.g. aggression, impulsivity and self injurious behaviours) are prominent. Risperidone tablets are also effective in maintaining the clinical improvement during continuation therapy in children and adolescents who have shown an initial treatment response. Pharmacological treatment should be an integral part of a more comprehensive treatment program, including psychosocial and educational intervention. Treatment with Risperidone tablets for patients with disruptive behaviour disorders should be initiated only in consultation with a specialist, including child and adolescent psychiatrists, paediatric neurologists,

developmental paediatricians, or other physicians conversant in the diagnosis and treatment of conduct and other disruptive behaviour disorders.

Risperidone tablets are indicated for the treatment of autism in children and adolescents.

Dosage and Administration

Schizophrenia

Switching from other antipsychotics

When medically appropriate, gradual discontinuation of the previous treatment while Risperidone tablet therapy is initiated is recommended. Also if medically appropriate, when switching patients from depot antipsychotics, initiate Risperidone tablet therapy in place of the next scheduled injection. The need for continuing existing anti-Parkinson medications should be re-evaluated periodically.

Adults

Risperidone tablets may be given once daily or twice daily. Patients should start with 2 mg/day Risperidone tablets. The dose may be increased on the second day to 4 mg. From then on the dosage can be maintained unchanged, or further individualised, if needed. Most patients will benefit from daily doses between 4 and 6 mg. In some patients a slower titration phase and a lower starting and maintenance dose may be appropriate.

Doses above 10 mg/day have not been shown to be superior in efficacy to lower doses and may cause extrapyramidal symptoms. Since the safety of doses above 16 mg/day has not been evaluated, doses above this level should not be used.

A benzodiazepine may be added to risperidone therapy when additional sedation is required.

Elderly

A starting dose of 0.5 mg twice daily is recommended. This dosage can be individually adjusted with 0.5 mg twice daily increments to 1 - 2 mg twice daily. Risperidone tablets are well tolerated in the elderly.

Children

Experience is lacking in children aged less than 15 years.

Bipolar Mania

Risperidone tablets should be administered on a once daily schedule, starting with 2mg. Dosage adjustments, if indicated, should occur at intervals of not less than 24 hours and in dosage increments of 1mg per day. A dosing range between 2 and 6mg per day is recommended. As with all symptomatic treatments, the continued use of Risperidone tablets must be evaluated and justified on an ongoing basis.

Behavioural Disturbances in Patients with Dementia

A starting dose of 0.25 mg twice daily is recommended. This dosage can be individually adjusted by increments of 0.25 mg twice daily, not more frequently than every other day, if needed. The optimum dose is 0.5 mg twice daily for most patients. Some patients, however, may benefit from doses up to 1 mg twice daily.

Once patients have reached their target dose, a once daily dosing regimen can be considered. As with all symptomatic treatments, the continued use of Risperidone tablets must be evaluated and justified on an on-going basis.

Conduct and other disruptive behaviour disorders

For subjects >50kg

A starting dose of 0.5mg once daily is recommended. This dosage can be individually adjusted by increments of 0.5mg once daily not more frequently than every other day, if needed. The optimum dose is 1mg once daily for most patients. Some patients, however, may benefit from 0.5mg once daily while others may require 1.5mg once daily.

For subjects <50kg

A starting dose of 0.25mg once daily is recommended, which can be individually adjusted by increments of 0.25mg once daily not more frequently than every other day, if needed. The optimum dose is 0.5mg once daily for most patients, although some patients may benefit from 0.25mg once daily while others may require 0.75mg once daily.

As with all symptomatic treatments, the continued use of Risperidone tablets must be evaluated and justified on an on-going basis.

Autism

Risperidone tablets can be administered once or twice daily. Patients experiencing somnolence may benefit from a switch in dosing from once daily to either once daily at bedtime, or twice daily.

Risperidone tablets should be administered based on body weight. Dosing should begin at 0.25 mg or 0.5 mg/day based upon weight (see Table 2 below for relative weight categories). On Day 4 of treatment, the dose may be increased up to 0.5 mg or 1.0mg/day. This dose should be maintained and response assessed at approximately day 14. Only in patients not achieving sufficient clinical response should additional dose increases be considered. Dose increases may proceed at ≥ 2 -week intervals in increments of 0.25 mg for patients <20 kg or 0.5 mg for patients ≥ 20 kg. Based upon current studies, the maximum dose studied did not exceed a total daily dose of 1.5 mg in patients <20 kg, 2.5 mg in patients ≥ 20 kg and 3.5 mg in patients >45 kg.

The table of the maximum daily doses provides a reference for titration and dosing by weight based upon current studies, and may serve as a guide according to clinical need:

Doses of Risperidone tablets in Paediatric Patients with Autistic Disorder				
Weight Categories	Days 1 - 3	Days 4 - 14+	Increments if dose increases are needed	Dose Range
Dose by Weight in mg/day				
< 20 kg	0.25 mg	0.5 mg	+0.25 mg at ≥ 2 week intervals	0.5 mg-1.5 mg
≥ 20 kg	0.5 mg	1.0 mg	+0.5 mg at ≥ 2 week intervals	1.0 mg-2.5 mg*

Dose Range in mg/kg/day

Doses of Risperidone tablets in Paediatric Patients with Autistic Disorder				
Weight Categories	Days 1 - 3	Days 4 - 14+	Increments if dose increases are needed	Dose Range
			Increments if dose increases are needed	Dose Range
All	0.01 mg/kg/d	0.02 mg/kg/d	+0.01 mg/kg/day at ≥ 2 week intervals	0.02 mg/kg/d-0.06 mg/kg/d

* Subjects weighing >45 kg may require higher doses: maximum dose studied was 3.5 mg/day

Once sufficient response has been achieved and maintained consideration may be given to gradually lowering the dose to achieve optimum balance of effectiveness and tolerance.

Clinical experience was limited in autistic adolescents and in autistic children with an IQ>84 as not many of these patients were included in the trials.

As with all symptomatic treatments, the continued use of Risperidone tablets in children and adolescents with autism must be evaluated and justified on an ongoing basis.

Renal and Hepatic Impairment

Patients with renal impairment have less ability to eliminate risperidone plus 9-hydroxy risperidone than normal adults. Patients with impaired hepatic function have increases in plasma concentration of the unbound risperidone.

Irrespective of the indication, starting and consecutive dosing should be halved, and dose titration should be slower for patients with renal or hepatic impairment. Risperidone tablets should be used with caution in these groups of patients.

Contraindications

Risperidone tablets are contraindicated in patients with a known hypersensitivity to the product.

Warnings and Precautions

Warnings

Elderly Patients with Dementia

Overall Mortality

Elderly patients with dementia treated with atypical antipsychotic drugs have an increased mortality compared to placebo in a meta-analysis of 17 controlled trials of atypical antipsychotic drugs, including Risperidone tablets. In placebo-controlled trials with Risperidone tablets in this population, the incidence of mortality was 4.0% (40/1009) for Risperidone tablets treated patients compared to 3.1% (22/712) for placebo-treated patients. The mean age (range) of patients who died was 86 years (range 67-100).

Concomitant use with Frusemide

In the Risperidone tablets placebo-controlled trials in elderly patients with dementia, a higher incidence of mortality was observed in patients treated with frusemide plus risperidone (7.3% [15/206]; mean age 89 years, range 75-97) when compared to patients treated with risperidone alone (3.1% [25/803]; mean age 84 years, range 70-96) or frusemide alone (4.1% [5/121]; mean age 80 years, range 67-90). The increase in mortality in patients treated with frusemide plus risperidone was observed in two of the four clinical trials.

No pathophysiological mechanism has been clearly identified to explain this finding, and no consistent pattern for cause of death was observed. Nevertheless, caution should be exercised and the risks and benefits of this combination should be considered prior to the decision to use. There was no increased mortality among patients taking other diuretics concomitantly with risperidone. Irrespective of treatment, dehydration was an overall risk factor for mortality and should therefore be carefully avoided in elderly patients with dementia.

Cerebrovascular Adverse Events

In placebo-controlled trials in elderly patients with dementia, there was a significantly higher incidence of cerebrovascular adverse events, such as stroke (including fatalities) and transient ischaemic attacks in patients (mean age 85 years, range 73-97) treated with Risperidone tablets compared with patients treated with placebo. The pooled data from six placebo-controlled studies in mainly elderly patients (>65 years of age) with dementia showed that cerebrovascular adverse events (serious and non-serious combined) occurred in 3.3% (33/989) of patients treated with risperidone and 1.2% (8/693) of patients treated with placebo. The Odds Ratio (95% exact confidence interval) was 2.96 (1.33, 7.45).

Risperidone may interfere with activities requiring mental alertness. Therefore, patients should be advised not to drive or operate machinery until their individual susceptibility is known.

Precautions

Due to the alpha-blocking activity of risperidone, orthostatic hypotension can occur, especially during the initial dose-titration period. Clinically significant hypotension has been observed postmarketing with concomitant use of risperidone and antihypertensive treatment. Risperidone tablets should be used with caution in patients with known cardiovascular disease (eg. heart failure, myocardial infarction, conduction abnormalities, dehydration, hypovolaemia, or cerebrovascular disease), and the dosage should be gradually titrated as recommended (see Dosage and Administration). A dose reduction should be considered if hypotension occurs. Special care should be taken in patients taking medications to lower blood pressure.

Tardive Dyskinesia

Medicines with dopamine receptor antagonistic properties have been associated with the induction of tardive dyskinesia characterised by rhythmical involuntary movements, predominantly of the tongue and/or face. It has been reported that the occurrence of extrapyramidal symptoms is a risk factor for the development of tardive dyskinesia. Because Risperidone tablets have a lower potential to induce extrapyramidal symptoms than classic neuroleptics, it should have a reduced risk of inducing tardive dyskinesia. If signs and symptoms of tardive dyskinesia appear, the discontinuation of all antipsychotic medicines should be considered.

Neuroleptic Malignant Syndrome

The Neuroleptic Malignant Syndrome, characterised by hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated creatine phosphokinase (CPK) levels has been reported to occur with classical neuroleptics. In this event, all antipsychotic medicines, including Risperidone tablets, should be discontinued.

Physicians should weigh the risks versus benefits when prescribing antipsychotics including Risperidone tablets to patients with Parkinson's disease or Dementia with Lewy Bodies (DLB) since both groups may be at increased risk of Neuroleptic Malignant Syndrome as well as having an increased sensitivity to antipsychotic medications. Manifestation of this increased sensitivity can include confusion, obtundation, postural instability with frequent falls, in addition to extrapyramidal symptoms.

Hyperglycaemia and Diabetes Mellitus

Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including Risperidone tablets. 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 hyperglycaemia related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycaemia-related adverse events in patients treated with atypical antipsychotics. Precise risk estimates for hyperglycaemia 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 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 should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycaemia including polydipsia, polyuria, polyphagia and weakness. Patients who develop symptoms of hyperglycaemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycaemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of antidiabetic treatment despite discontinuation of the suspect drug.

QT Interval

As with other antipsychotics, caution should be exercised when risperidone is prescribed in patients with a history of cardiac arrhythmias, in patients with congenital long QT syndrome, and in concomitant use with drugs known to prolong the QT interval.

Dysphagia

Oesophageal 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. Risperidone and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

Other Precautions

Classical neuroleptics are known to lower the seizure threshold. Caution is recommended when treating patients with epilepsy.

Patients may be advised to refrain from excessive eating in view of the possibility of weight gain.

Use in the Elderly

It is recommended to halve both the starting dose and the subsequent dose increments in geriatric patients.

Use in Renal Impairment

It is recommended to halve both the starting dose and the subsequent dose increments in patients with renal insufficiency.

Use in Hepatic Impairment

It is recommended to halve both the starting dose and the subsequent dose increments in patients with hepatic insufficiency.

Use in Pregnancy and Lactation

The safety of Risperidone tablets for use during human pregnancy has not been established. Reversible extrapyramidal symptoms in the neonate were observed following postmarketing use of risperidone during the last trimester of pregnancy. Although, in experimental animals, risperidone did not show direct reproductive toxicity, some indirect, prolactin- and CNS-mediated effects were observed. No teratogenic effect of risperidone was noted in any study. Therefore, Risperidone tablets should only be used during pregnancy if the benefits outweigh the risks.

In animal studies, risperidone and 9-hydroxyrisperidone are excreted in the milk. It has been demonstrated that this excretion also occurs in human breast milk.

Therefore, women receiving Risperidone tablets should not breast feed.

Paediatric Use

Risperidone tablets had no adverse effects on cognitive function in paediatric patients. In combined, long-term, open-label trials, mean changes in cognitive function tests were small and did not increase or decrease over time.

A mean increase of 7.5 kg after 12 months of Risperidone tablet treatment was observed, somewhat higher than the expected weight gain (approximately 3 to 3.5 kg per year) for children predominantly between 5 and 12 years of age.

Risperidone tablet treatment for up to 3 years showed no adverse effects on growth and sexual maturation. No differences were observed between risperidone and placebo groups in measurements of sexual maturation, using the Tanner scale, and no adverse events suggestive of delayed pubertal maturation were reported. The mean change in height after 1 year of treatment with risperidone was within the expected growth range in this population.

Experience of risperidone treatment in children with schizophrenia aged less than 15 years is lacking. Experience is lacking in children with conduct and other disruptive behaviour disorders aged less than 5 years. Experience is lacking in children with autism aged less than 5 years.

Adverse Effects

The most frequently reported ADRs (incidence \geq 10%) are: Parkinsonism, Headache, and Insomnia.

The following are all the ADRs that were reported in clinical trials and post-marketing. The following terms and frequencies are applied: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1000$), very rare ($< 1/10,000$), and not known (cannot be estimated from the available clinical trial data).

Adverse Drug Reactions by System Organ Class and Frequency	
Infections and infestations	
Common	Nasopharyngitis, Upper respiratory tract infection, Urinary tract infection, Influenza, Rhinitis, Bronchitis, Pneumonia
Uncommon	Sinusitis, Viral infection, Pharyngitis, Ear infection, Tonsillitis, Cellulitis, Otitis media, Eye infection, Localised infection, Acarodermatitis, Respiratory tract infection, Cystitis, Onychomycosis, Bronchopneumonia
Rare	Otitis media chronic, Tracheobronchitis
Blood and lymphatic disorders	
Uncommon	Anaemia, Thrombocytopenia
Rare	Granulocytopenia
Not known	Agranulocytosis
Immune system disorders	
Uncommon	Hypersensitivity
Rare	Drug hypersensitivity
Not known	Anaphylactic reaction
Endocrine disorders	
Uncommon	Hyperprolactinemia
Rare	Inappropriate antidiuretic hormone secretion
Metabolism and nutrition disorders	
Common	Increased appetite, Decreased appetite
Uncommon	Anorexia, Polydipsia
Very rare	Diabetic ketoacidosis
Not known	Water intoxication
Psychiatric disorders	
Very common	Insomnia
Common	Agitation, Anxiety, Sleep disorder
Uncommon	Confusional state, Mania, Nervousness, Libido decreased, Middle insomnia, Listless
Rare	Anorgasmia, Blunted affect
Nervous system disorders	
Very common	Parkinsonism, Headache
Common	Somnolence, Akathisia, Sedation, Dizziness, Tremor, Dystonia, Lethargy, Dyskinesia

Adverse Drug Reactions by System Organ Class and Frequency

Uncommon	Drooling, Dysarthria, Disturbance in attention, Hypersomnia, Dizziness postural, Syncope, Balance disorder, Tardive dyskinesia, Depressed level of consciousness, Speech disorder, Cerebrovascular accident, Coordination abnormal, Unresponsive to stimuli, Hypoaesthesia, Transient ischemic attack, Loss of consciousness
Rare	Cerebral ischemia, Cerebrovascular disorder, Movement disorder, Neuroleptic malignant syndrome, Diabetic coma

Eye disorders

Common	Vision blurred
Uncommon	Conjunctivitis, Ocular hyperaemia, Eye discharge, Eye swelling, Dry eye, Eyelid oedema, Lacrimation increased, Photophobia
Rare	Eyelid margin crusting, Visual acuity reduced, Eye rolling, Glaucoma

Ear and labyrinth disorders

Uncommon	Ear pain, Tinnitus
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Cardiac disorders

Common	Tachycardia
Uncommon	Palpitations, Sinus tachycardia, Atrial fibrillation, Sinus bradycardia, Atrioventricular block first degree, Bundle branch block left
Rare	Bundle branch block right, Atrioventricular block

Vascular disorders

Uncommon	Hypotension, Orthostatic hypotension, Flushing
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Respiratory, thoracic, and mediastinal disorders

Common	Cough, Nasal congestion, Pharyngolaryngeal pain, Epistaxis, Rhinorrhea, Dyspnea
Uncommon	Wheezing, Sinus congestion, Productive cough, Dysphonia, Respiratory tract congestion, Pulmonary congestion, Pneumonia aspiration, Respiratory disorder, Rales
Rare	Hyperventilation, Nasal oedema, Sleep apnea syndrome

Gastrointestinal disorders

Common	Vomiting, Constipation, Nausea, Diarrhoea, Salivary hypersecretion, Abdominal pain upper, Dyspepsia, Dry mouth, Abdominal pain, Stomach discomfort
Uncommon	Dysphagia, Abdominal discomfort, Gastritis, Faecal incontinence, Faecaloma
Rare	Lip swelling, Cheilitis, Intestinal obstruction, Aptyalism

Hepatobiliary disorders

Rare	Jaundice
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Skin and subcutaneous tissue disorders

Adverse Drug Reactions by System Organ Class and Frequency

Common	Rash, Erythema
Uncommon	Dry skin, Pruritis, Acne, Skin lesion, Skin discolouration, Angioedema, Hyperkeratosis, Rash erythematous, Skin disorder, Seborrhoeic dermatitis
Rare	Dandruff, Rash papular, Rash maculo-papular, Rash generalised

Musculoskeletal, connective tissue, and bone disorders

Common	Arthralgia, Back pain, Pain in extremity
Uncommon	Myalgia, Neck pain, Joint swelling, Posture abnormal, Joint stiffness, Muscular weakness, Musculoskeletal chest pain
Rare	Rhabdomyolysis

Renal and urinary disorders

Common	Enuresis
Uncommon	Urinary incontinence, Dysuria, Pollakiuria

Reproductive system and breast disorders

Uncommon	Erectile dysfunction, Galactorrhea, Amenorrhea, Gynecomastia, Ejaculation failure, Ejaculation disorder, Menstruation irregular, Vaginal discharge, Sexual dysfunction
Rare	Retrograde ejaculation, Menstrual disorder, Breast enlargement
Not known	Priapism

General disorders and administration site conditions

Common	Fatigue, Pyrexia, Oedema peripheral, Asthenia, Chest pain
Uncommon	Gait disturbance, Sluggishness, Malaise, Influenza like illness, Pitting oedema, Oedema, Thirst, Chest discomfort, Chills, Feeling abnormal, Discomfort, Face oedema
Rare	Peripheral coldness, Drug withdrawal syndrome, Adverse drug reaction, Generalised oedema, Hypothermia

Investigations

Common	Weight increased, Blood prolactin increased
Uncommon	Body temperature increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Heart rate increased, White blood cell count decreased, Blood glucose increased, Blood creatine phosphokinase increased, Electrocardiogram abnormal, Eosinophil count increased, Hemoglobin decreased, Electrocardiogram QT prolonged, Hematocrit decreased, Blood pressure decreased
Rare	Transaminases increased, Body temperature decreased

Additional Information on Special Populations

Elderly patients with dementia:

Transient ischaemic attack and cerebrovascular accident were ADRs reported in clinical trials with a frequency of 1.4% and 1.5%, respectively, in elderly patients with

dementia. In addition, the following ADRs were reported with a frequency $\geq 5\%$ in elderly patients with dementia and with at least twice the frequency seen in other adult populations: urinary tract infection, peripheral oedema, lethargy, and cough.

Paediatric patients:

The following ADRs were reported with a frequency $\geq 5\%$ in paediatric patients (5 to 17 years) and with at least twice the frequency seen in clinical trials in adults: somnolence/sedation, fatigue, headache, increased appetite, vomiting, dizziness, upper abdominal pain, cough, pyrexia, tremor, diarrhoea, and enuresis.

Interactions

Given the primary CNS effects of risperidone, it should be used with caution in combination with other centrally-acting medicines.

Risperidone may antagonise the effects of levodopa and other dopamine agonists. Clinically significant hypotension has been observed postmarketing with concomitant use of risperidone and antihypertensive treatment.

Caution is advised when prescribing Risperidone tablets with drugs known to prolong the QT interval.

Carbamazepine has been shown to decrease the plasma levels of risperidone plus 9-hydroxy risperidone. Similar effects may be observed with other CYP 3A4 hepatic enzyme inducers. When carbamazepine or other CYP 3A4 hepatic enzyme inducers are initiated or discontinued, the physician should re-evaluate the dosing of Risperidone tablets.

Fluoxetine and paroxetine, CYP 2D6 inhibitors, increase the plasma concentration of risperidone, but less so of risperidone plus 9-hydroxy risperidone. When concomitant fluoxetine or paroxetine is initiated or discontinued, the physician should re-evaluate the dosing of Risperidone tablets.

Topiramate modestly reduced the bioavailability of risperidone, but not that of risperidone plus 9-hydroxy risperidone. Therefore, this interaction is unlikely to be of clinical significance.

Phenothiazines, tricyclic antidepressants and some beta-blockers may increase the plasma concentrations of risperidone but not those of risperidone plus 9-hydroxy risperidone. Amitriptyline does not affect the pharmacokinetics of risperidone or risperidone plus 9-hydroxy risperidone. Cimetidine and ranitidine increased the bioavailability of risperidone but only marginally that of risperidone plus 9-hydroxy risperidone.

Erythromycin, a CYP3A4 inhibitor, does not change the pharmacokinetics of risperidone and risperidone plus 9-hydroxy risperidone. The cholinesterase inhibitors galantamine and donepezil do not show a clinically relevant effect on the pharmacokinetics of risperidone and risperidone plus 9-hydroxy risperidone. When risperidone is taken together with other highly protein-bound medicines, there is no clinically relevant displacement of either medicine from the plasma proteins.

Risperidone tablets do not show a clinically relevant effect on the pharmacokinetics of lithium, valproate, digoxin or topiramate.

See Precautions section (Elderly Patients with Dementia) regarding increased mortality in elderly dementia patients concomitantly receiving frusemide.

Food does not affect the absorption of Risperidone tablets.

Overdosage

Symptoms

In general, reported signs and symptoms have been those resulting from an exaggeration of the known pharmacological effects of Risperidone tablets. These include drowsiness and sedation, tachycardia and hypotension, and extrapyramidal symptoms. In overdose, QT prolongation and convulsions have been reported. Torsade de pointes has been reported in association with combined overdose of oral risperidone and paroxetine.

In case of acute overdosage, the possibility of multiple medicine involvement should be considered.

Treatment

Establish and maintain a clear airway and ensure adequate oxygenation and ventilation. Gastric lavage (after intubation, if the patient is unconscious) and administration of activated charcoal together with a laxative should be considered. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias.

There is no specific antidote to Risperidone tablets. Therefore appropriate supportive measures should be instituted. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents. In case of severe extrapyramidal symptoms, anticholinergic medication should be administered. Close medical supervision and monitoring should continue until the patient recovers.

As strategies for the management of overdose are continually evolving, it is advisable to contact the Poisons Information Centre to determine the latest recommendations for the management of an overdose

Pharmaceutical Precautions

Risperidone tablets should be stored below 30°C.

Medicine Classification

Prescription Medicine

Package Quantities

Risperidone tablets 1, 2, 3 and 4 mg - blisters in cartons of 30 or 60 tablets.

Risperidone tablets 0.5 - blisters in cartons of 10, 20, 30 or 60 tablets.

Not all pack sizes may be available.

Further Information

Excipients

The 0.5 mg tablets contain lactose, starch, microcrystalline cellulose, talc, hypromellose, magnesium stearate, colloidal anhydrous silica, sodium lauryl sulphate, titanium dioxide, red iron oxide (E171) and propylene glycol.

The 1 mg tablets contain lactose, starch, microcrystalline cellulose, talc, hypromellose, magnesium stearate, colloidal anhydrous silica, sodium lauryl sulphate, titanium dioxide and propylene glycol.

The 2 mg tablets contain lactose, starch, microcrystalline cellulose, talc, hypromellose, magnesium stearate, colloidal anhydrous silica, sodium lauryl sulphate, propylene glycol, titanium dioxide, sunset yellow (CI 15985) and quinoline yellow.

The 3 mg tablets contain lactose, starch, microcrystalline cellulose, talc, hypromellose, magnesium stearate, colloidal anhydrous silica, sodium lauryl sulphate, propylene glycol, titanium dioxide, and quinoline yellow.

The 4 mg tablets contain lactose, starch, microcrystalline cellulose, talc, hypromellose, magnesium stearate, colloidal anhydrous silica, sodium lauryl sulphate, propylene glycol, titanium dioxide, quinoline yellow and FD&C Blue #2.

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Date of Preparation

26 October 2009