Rischotic®

Risperidone

FORMS AND PRESENTATION

Rischotic® 0.25: Film coated tablets: Box of 20.
Rischotic® 0.5: Film coated tablets: Box of 20.
Rischotic® 1: Film coated tablets: Box of 20.
Rischotic® 2: Film coated tablets: Box of 20.
Rischotic® 3: Film coated tablets: Box of 20.
Rischotic® 4: Film coated tablets: Box of 20.

COMPOSITION

Rischotic® 0.25: Each film coated tablet contains Risperidone 0.25mg.
Rischotic® 0.5: Each film coated tablet contains Risperidone 0.5mg.
Rischotic® 1: Each film coated tablet contains Risperidone 1mg.
Rischotic® 2: Each film coated tablet contains Risperidone 2mg.
Rischotic® 3: Each film coated tablet contains Risperidone 3mg.
Rischotic® 4: Each film coated tablet contains Risperidone 4mg.
Excipients: starch, microcrystalline cellulose, colloidal silicon dioxide, lactose, magnesium stearate, hydroxypropyl methylcellulose, titanium dioxide, propylene glycol, talc, yellow iron oxide (Rischotic® 0.25), red iron oxide (Rischotic® 0.5), FD&C yellow (Rischotic® 2), D&C yellow (Rischotic® 3 , Rischotic® 4), FD&C blue (Rischotic® 4).

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Therapeutic class: Psycholeptics.
ATC code: N05AX08.
Risperidone is a selective monoaminergic antagonist with unique properties. It has a high affinity for serotonergic 5-HT_2 and dopaminergic D_2 receptors. Risperidone binds also to alpha1-adrenergic receptors, and, with lower affinity, to H_1-histaminergic and $alpha_2$-adrenergic receptors. Risperidone has no affinity for cholinergic receptors. Although Risperidone is a potent D_2 antagonist, which is considered to improve the positive symptoms of schizophrenia, it causes less depression of motor activity and induction of catalepsy than classical antipsychotics. Balanced central serotonin and dopamine antagonism may reduce extrapyramidal side effects liability and extend the therapeutic activity to the negative and affective symptoms of schizophrenia.

Pharmacokinetic properties

Absorption
Risperidone is completely absorbed after oral administration, reaching peak plasma concentrations within 1 to 2 hours. The absolute oral bioavailability of Risperidone is 70% (CV=25%). The relative oral bioavailability of Risperidone from a tablet is 94% (CV=10%) compared with a solution. The absorption is not affected by food and thus Risperidone can be given with or without meals. 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.
Distribution
Risperidone is rapidly distributed. The volume of distribution is 1-2 l/kg. In plasma, Risperidone is bound to albumin and $alpha_1$-acid glycoprotein. The plasma protein binding of Risperidone is 90%, that of 9-hydroxy-risperidone is 77%.
Risperidone plasma concentrations are dose-proportional within the therapeutic dose-range.
Biotransformation
Risperidone is metabolized by CYP 2D6 to 9-hydroxy-risperidone, which has a similar pharmacological activity as Risperidone. Risperidone plus 9-hydroxy-risperidone form the active antipsychotic fraction. CYP 2D6 is subject to genetic polymorphism. Extensive CYP 2D6 metabolizers convert Risperidone rapidly into 9-hydroxy-risperidone, whereas poor CYP 2D6 metabolizers convert it much more slowly. Although extensive metabolizers have lower Risperidone and higher 9-hydroxy-risperidone concentrations than poor metabolizers, the pharmacokinetics of Risperidone and 9-hydroxy-risperidone combined (i.e., the active antipsychotic fraction), after single and multiple doses, are similar in extensive and poor metabolizers of CYP 2D6.
Another metabolic pathway of Risperidone is N-dealkylation. In vitro studies in human liver microsomes showed that Risperidone at clinically relevant concentration does not substantially inhibit the metabolism of medicines metabolized by cytochrome P450 isozymes, including CYP 1A2, CYP 2A6, CYP 2C8/9/10, CYP 2D6, CYP 2E1, CYP 3A4, and CYP 3A5.
Elimination
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 35-45% of the dose. The remainder is inactive metabolites. 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 the active antipsychotic fraction is 24 hours.

INDICATIONS

Rischotic® is indicated:
- For the treatment of schizophrenia.
- For the treatment of moderate to severe manic episodes associated with bipolar disorders.
- For the short-term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer's dementia unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others.
- For the short-term symptomatic treatment (up to 6 weeks) of persistent aggression in conduct disorder in children from the age of 5 years and adolescents with sub average intellectual functioning or mental retardation diagnosed according to DSM-IV criteria, in whom the severity of aggressive or other disruptive behaviors require pharmacologic treatment. Pharmacological treatment should be an integral part of a more comprehensive treatment program, including psychosocial and educational intervention. It is recommended that Rischotic® be prescribed by a specialist in child neurology and child and adolescent psychiatry or physicians well familiar with the treatment of conduct disorder of children and adolescents.

CONTRAINDICATIONS

- Hypersensitivity to Risperidone or to any of the excipients.

PRECAUTIONS

- Elderly patients with dementia: Increased mortality in elderly people with dementia was observed. There is insufficient data to give a firm estimate of the precise magnitude of the risk and the cause of the increased risk is not known.
- Concomitant use with Furosemide: The increase in mortality in patients treated with furosemide plus Risperidone was observed in two of four clinical trials. Concomitant use of Risperidone with other diuretics (mainly thiazide diuretics used in low dose) was not associated with similar findings.
No pathophysiological mechanism has been identified to explain this finding, and no consistent pattern for cause of death observed. Nevertheless, caution should be exercised and the risks and benefits of this combination or co-treatment with other potent diuretics should be considered prior to the decision to use. There was no increased incidence of mortality among patients taking other diuretics as concomitant medication 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 (CVAE): An approximately 3-fold increased risk of cerebrovascular adverse events has been seen in randomized placebo controlled clinical trials in the dementia population with some atypical antipsychotics. The mechanism for this increased risk is not known. An increased risk cannot be excluded for other antipsychotics or other patient populations. Risperidone should be used with caution in patients with risk factors for stroke.
The risk of CVAEs was significantly higher in patients with mixed or vascular type of dementia when compared to Alzheimer's dementia. Therefore, patients with other types of dementias than Alzheimer's should not be treated with Risperidone.
Physicians are advised to assess the risks and benefits of the use of Risperidone in elderly patients with dementia, taking into account risk predictors for stroke in the individual patient. Patients/caregivers should be cautioned to immediately report signs and symptoms of potential CVAEs such as sudden weakness or numbness in the face, arms or legs, and speech or vision problems. All treatment options should be considered without delay, including discontinuation of Risperidone.
Risperidone should only be used short term for persistent aggression in patients with moderate to severe Alzheimer's dementia to supplement non-pharmacological approaches which have had limited or no efficacy and when there is potential risk of harm to self or others.
Patients should be reassessed regularly, and the need for continuing treatment reassessed.
- Orthostatic hypotension: Due to the alpha-blocking activity of Risperidone, (orthostatic) hypotension can occur, especially during the initial dose-titration period. Risperidone should be used with caution in patients with known cardiovascular disease (e.g., heart failure, myocardial infarction, conduction abnormalities, dehydration, hypovolemia, or cerebrovascular disease), and the dosage should be gradually titrated as recommended. A dose reduction should be considered if hypotension occurs.
- Tardive Dyskinesia/Extrapyramidal Symptoms (TD/EPS): Medicinal products with dopamine receptor antagonist properties have been associated with the induction of tardive dyskinesia, characterized by rhythmical involuntary movements, predominantly of the tongue and/or face.
The onset of extrapyramidal symptoms is a risk factor for tardive dyskinesia. If signs and symptoms of tardive dyskinesia appear, the discontinuation of all antipsychotics should be considered.
- Neuroleptic Malignant Syndrome (NMS): Neuroleptic Malignant Syndrome, characterized by hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated serum creatine phosphokinase levels has been reported to occur with antipsychotics. Additional signs may include myoglobinuria (rhabdomyolysis) and acute renal failure. In this event, all antipsychotics, including Risperidone, should be discontinued.
- Parkinson's disease and Dementia with Lewy Bodies (DLB): Physicians should weigh the risks versus the benefits when prescribing antipsychotics, including Risperidone, to patients with Parkinson's disease or Dementia with Lewy Bodies. Parkinson's disease may worsen with Risperidone. Both groups may be at increased risk of Neuroleptic Malignant Syndrome as well as having an increased sensitivity to antipsychotic medicinal products; these patients were excluded from clinical trials. Manifestation of this increased sensitivity can include confusion, obtundation, and postural instability with frequent falls, in addition to extrapyramidal symptoms.
- Hyperglycemia and diabetes mellitus: Hyperglycemia, diabetes mellitus and exacerbation of pre-existing diabetes have been reported during treatment with Risperidone. In some cases, a prior increase in body weight has been reported which may be a predisposing factor. Association with ketoacidosis has been reported very rarely, and rarely with diabetic coma. Appropriate clinical monitoring is advisable in accordance with utilized antipsychotic guidelines. Patients treated with any atypical antipsychotic including Risperidone should be monitored for symptoms of hyperglycemia (such as polydipsia, polyuria, polyphagia and weakness) and patients with diabetes mellitus should be monitored regularly for worsening of glucose control.
- Weight gain: Significant weight gain has been reported with Risperidone use. Weight should be monitored regularly.
- Hyperprolactinemia: Tissue culture studies suggest that cell growth in human breast tumors may be stimulated by prolactin. Although no clear association with the administration of antipsychotics has so far been demonstrated in clinical and epidemiological studies, caution is recommended in patients with relevant medical history. Risperidone should be used with caution in patients with pre-existing hyperprolactinemia and in patients with possible prolactin-dependent tumors.
- QT prolongation: QT prolongation has very rarely been reported postmarketing. As with other antipsychotics, caution should be exercised when Risperidone is prescribed in patients with known cardiovascular disease, family history of QT prolongation, bradycardia, or electrolyte disturbances (hypokalemia, hypomagnesemia), as it may increase the risk of arrhythmogenic effects, and in concomitant use with medicines known to prolong the QT interval.
- Seizure: Risperidone should be used cautiously in patients with a history of seizures or other conditions that potentially lower the seizure threshold.
- Priapism: Priapism may occur with Risperidone treatment due to its alpha-adrenergic blocking effects.
- Venous thromboembolism (VTE): Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with Risperidone tablets and preventive measures undertaken.
- Body temperature regulation: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic medicines. Appropriate care is advised when prescribing Risperidone to patients who will be experiencing conditions which may contribute to an elevation in core body temperature, e.g., exercising strenuously, exposure to extreme heat, receiving concomitant treatment with anticholinergic activity, or being subject to dehydration.
- Children and adolescents: Before Risperidone is prescribed to a child or adolescent with conduct disorder they should be fully assessed for physical and social causes of the aggressive behavior such as pain or inappropriate environmental demands.
The sedative effect of Risperidone should be closely monitored in this population because of possible consequences on learning ability. A change in the time of administration of Risperidone could improve the impact of the sedation on attention faculties of children and adolescents.
Risperidone was associated with mean increases in body weight and body mass index (BMI). Changes in height were within expected age-appropriate norms. The effect of long-term Risperidone treatment on sexual maturation and height has not been adequately studied.
Because of the potential effects of prolonged hyperprolactinemia on growth and sexual maturation in children and adolescents, regular clinical evaluation of endocrinological status should be considered, including measurements of height, weight, sexual maturation, monitoring of menstrual functioning, and other potential prolactin-related effects.
During treatment with Risperidone regular examination for extrapyramidal symptoms and other movement disorders should also be conducted.
- Lactose: The film coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medication.

Ability to drive and use machines

Risperidone can have minor or moderate influence on the ability to drive and use machines due to potential nervous system and visual effects. Therefore, patients should be advised not to drive or operate machinery until their individual susceptibility is known.

PREGNANCY AND LACTATION

There are no adequate data from the use of Risperidone in pregnant women.
According to postmarketing data reversible extrapyramidal symptoms in the neonate were observed following the use of Risperidone during the last trimester of pregnancy. Consequently newborns should be monitored carefully. Risperidone was not teratogenic in animal studies but other types of reproductive toxicity were seen. The potential risk for humans is unknown. Therefore, Risperidone should not be used during pregnancy unless clearly necessary. If discontinuation during pregnancy is necessary, it should not be done abruptly.
Neonates exposed to antipsychotics (including Risperidone) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

In animal studies, Risperidone and 9-hydroxy-risperidone are excreted in the milk. It has been demonstrated that Risperidone and 9-hydroxy-risperidone are also excreted in human breast milk in small quantities. There are no data available on adverse reactions in breast-feeding infants. Therefore, the advantage of breast-feeding should be weighed against the potential risks for the child.

DRUG INTERACTIONS

As with other antipsychotics, caution is advised when prescribing Risperidone with medicinal products known to prolong the QT interval, e.g., class Ia antiarrhythmics (e.g., quinidine, dysopiramide, procainamide), class III antiarrhythmics (e.g., amiodarone, sotalol), tricyclic antidepressant (i.e., amitriptyline), tetracyclic antidepressants (i.e., maprotiline), some antihistaminics, other antipsychotics, some antimalarials (i.e., chinice and mefloquine), and with medicines causing electrolyte imbalance (hypokalemia, hypomagnesiemia), bradycardia, or those which inhibit the hepatic metabolism of Risperidone. This list is indicative and not exhaustive.

Potential for Risperidone to affect other medicinal products

- Risperidone should be used with caution in combination with other centrally-acting substances notably including alcohol, opiates, antihistamines and benzodiazepines due to the increased risk of sedation.
- Risperidone may antagonize the effect of levodopa and other dopamine agonists. If this combination is deemed necessary, particularly in end-stage Parkinson's disease, the lowest effective dose of each treatment should be prescribed.
- Clinically significant hypotension has been observed postmarketing with concomitant use of Risperidone and antihypertensive treatment.
- Risperidone does not show a clinically relevant effect on the pharmacokinetics of lithium, valproate, digoxin or topiramate.

Potential for other medicinal products to affect Risperidone

- Carbamazepine has been shown to decrease the plasma concentrations of the active antipsychotic fraction of Risperidone. Similar effects may be observed with e.g. rifampicin, phenytoin and phenobarbital which also induce CYP 3A4 hepatic enzyme as well as P-glycoprotein. When carbamazepine or other CYP 3A4 hepatic enzyme/P-glycoprotein (P-gp) inducers are initiated or discontinued, the physician should re-evaluate the dosing of Risperidone.

Fluoxetine and paroxetine, CYP 2D6 inhibitors, increase the plasma concentration of Risperidone, but less so of the active antipsychotic fraction. It is expected that other CYP 2D6 inhibitors, such as quinidine, may affect the plasma concentrations of Risperidone in a similar way. When concomitant fluoxetine or paroxetine is initiated or discontinued, the physician should re-evaluate the dosing of Risperidone

- Verapamil, an inhibitor of CYP 3A4 and P-gp, increases the plasma concentration of Risperidone.
- Galantamine and donepezil do not show a clinically relevant effect on the pharmacokinetics of Risperidone and on the active antipsychotic fraction.
- Phenothiazines, tricyclic antidepressants, and some beta-blockers may increase the plasma concentrations of Risperidone but not those of the active antipsychotic fraction. Amitriptyline does not affect the pharmacokinetics of Risperidone or the active antipsychotic fraction. Cimetidine and ranitidine increase the bioavailability of Risperidone, but only marginally that of the active antipsychotic fraction. Erythromycin, a CYP 3A4 inhibitor, does not change the pharmacokinetics of Risperidone and the active antipsychotic fraction.
- The combined use of psychostimulants (e.g., methylphenidate) with Risperidone in children and adolescents did not alter the pharmacokinetics and efficacy of Risperidone.
- Concomitant use of oral Risperidone with paliperidone is not recommended as paliperidone is the active metabolite of Risperidone and the combination of the two may lead to additive active antipsychotic fraction exposure.

ADVERSE EFFECTS

The most frequently reported adverse drug reactions (ADRs) (incidence ≥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 (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1000 to < 1/100); rare (≥ 1/10000 to < 1/1000); very rare (< 1/10000), not known (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Adverse drug reactions are listed by system organ class and frequency.

- Investigations: Inscreased blood prolactin (Hyperprolactinemia can in some cases lead to gynecomastia, menstrual disturbances, amenorrhea, galactorrhea), increased weight (common); prolonged electrocardiogram QT, abnormal electrocardiogram, increased transaminases, decreased white blood cell count, increased body temperature, increased eosinophil count, decreased hemoglobin, increased blood creatine phosphokinase (uncommon); decreased body temperature (rare).
- Cardiac disorders: Tachycardia (common); atrioventricular block, bundle branch block, atrial fibrillation, sinus bradycardia, palpitations (uncommon).
- Blood and lymphatic system disorders: Anemia, thrombocytopenia (uncommon); granulocytopenia (rare); agranulocytosis (not known).
- Nervous system disorders: Parkinsonism (salivary hypersecretion, musculoskeletal stiffness, drooling, cogwheel rigidity, bradykinesia, hypokinesia, masked facies, muscle tightness, akinesia, nuchal rigidity, muscle rigidity, parkinsonian gait, and abnormal glabellar reflex), headache (very common); akathisia (restlessness, hyperkinesia, and restless leg syndrome), dizziness, tremor, dyskinesia (muscle twitching, choreoathetosis, athetosis, and myoclonus) , dystonia, somnolence, sedation, lethargy (common); unresponsive to stimuli, loss of consciousness, syncope, depressed level of consciousness, cerebrovascular accident, transient ischemic attack, dysarthria, disturbance in attention, hypersomnia, postural dizziness, balance disorder, tardive dyskinesia, speech disorder, abnormal coordination, hypoesthesia (uncommon); Neuroleptic Malignant Syndrome, diabetic coma, cerebrovascular disorder, cerebral ischemia, movement disorder (rare).
- Eye disorders: Blurred vision (common); conjunctivitis, ocular hyperemia, eye discharge, eye swelling, dry eye, increased lacrimation, photophobia (uncommon); reduced visual acuity, eye rolling, glaucoma (rare).
- Ear and labyrinth disorders: Ear pain, tinnitus (uncommon).
- Respiratory, thoracic and mediastinal disorders: Dyspnea, epistaxis, cough, nasal congestion, pharyngo-laryngeal pain (common); wheezing, pneumonia aspiration, pulmonary congestion, respiratory disorder, rales, respiratory tract congestion, dysphonia (uncommon); sleep apnea syndrome, hyperventilation (rare).
- Gastrointestinal disorders: Vomiting, diarrhea, constipation, nausea, abdominal pain, dyspepsia, dry mouth, stomach discomfort (common); dysphagia, gastritis, fecal incontinence, fecaloma (uncommon); intestinal obstruction, pancreatitis, lip swelling, cheilitis (rare).
- Renal and urinary disorders: Enuresis (common); urinary retention, dysuria, urinary incontinence, pollakiuria (uncommon).
- Skin and subcutaneous tissue disorders: Rash, erythema (common); angioedema, skin lesion, skin disorder, pruritus, acne, skin discoloration, alopecia, seborrheic dermatitis, dry skin, hyperkeratosis (uncommon); dandruff (rare).
- Musculoskeletal and connective tissue disorders: Arthralgia, back pain, pain in extremity (common); muscular weakness, myalgia, neck pain, joint swelling, abnormal posture, joint stiffness, musculoskeletal chest pain (uncommon); rhabdomyolysis (rare).
- Endocrine disorders: Inappropriate anti-diuretic hormone secretion (rare).
- Metabolism and nutrition disorders: Increased appetite, decreased appetite (common); diabetes mellitus, anorexia, polydipsia, hyperglycemia (uncommon); hypoglycemia (rare); diabetic ketoacidosis (very rare); water intoxication (not known).
- Infections and infestations: Pneumonia, influenza, bronchitis, upper respiratory tract infection, urinary tract infection (common); sinusitis, viral infection, ear infection, tonsillitis, cellulitis, otitis media, eye infection, localised infection, acarodermatitis, respiratory tract infection, cystitis, onychomycosis (uncommon); chronic otitis media (rare).
- Vascular disorders: Hypotension, orthostatic hypotension, flushing (uncommon).
- General disorders and administration site conditions: Pyrexia, fatigue, peripheral edema, asthenia, chest pain (common); face edema, gait disturbance, abnormal feeling, sluggishness, influenza like illness, thirst, chest discomfort, chills (uncommon); generalized edema, hypothermia, drug withdrawal syndrome, peripheral coldness (rare).
- Immune system disorders: Hypersensitivity (uncommon); drug hypersensitivity (rare); anaphylactic reaction (not known).
- Hepatobiliary disorders: Jaundice (rare).
- Reproductive system and breast disorders: Amenorrhea, sexual dysfunction, erectile dysfunction, ejaculation disorder, galactorrhea, gynecomastia, menstrual disorder, vaginal discharge (uncommon); priapism (not known).
- Psychiatric disorders: Insomnia (very common); anxiety, agitation, sleep disorder (common); confusional state, mania, decreased libido, listless, nervousness (uncommon); anorgasmia, blunted affect (rare).
- Pregnancy, puerperium and perinatal conditions: Neonatal drug withdrawal syndrome (not known).

DOSAGE AND ADMINISTRATION

Schizophrenia

- Adults: Rischotic® may be given once or twice daily.

Patient should start with 2 mg/day of Rischotic®. The dosage may be increased on the second day to 4 mg. Subsequently, the dosage can be maintained unchanged, or further individualized, 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 demonstrated superior efficacy to lower doses and may cause increased incidence of extrapyramidal symptoms.

Safety of doses above 16 mg/day has not been evaluated and are therefore not recommended.

- 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 to 2 mg twice daily.
- Pediatric population: Rischotic® is not recommended for use in children below age 18 with schizophrenia due to a lack of data on efficacy.

Manic episodes in bipolar disorder

- Adults: Rischotic® should be administered on a once daily schedule, starting with 2mg of Rischotic®. Dosage adjustments, if indicated, should occur at intervals of not less than 24 hours and in dosage increments of 1mg per day. Rischotic® can be administered in flexible doses over a range of 1 to 6 mg per day to optimize each patient's level of efficacy and tolerability. Daily doses over 6 mg of Rischotic® have not been investigated in patients with manic episodes.

As with all symptomatic treatments, the continued use of Rischotic® must be evaluated and justified on an ongoing basis.

- 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 to 2 mg twice daily. Since clinical experience in elderly is limited, caution should be exercised.
- Pediatric population: Rischotic® is not recommended for use in children below age 18 with bipolar mania due to a lack of data on efficacy.

Persistent aggression in patients with moderate to severe Alzheimer's 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.

Rischotic® should not be used more than 6 weeks in patients with persistent aggression in Alzheimer's dementia. During treatment, patients must be evaluated frequently and regularly, and the need for continuing treatment reassessed.

Conduct disorder

Children and adolescents from 5 to 18 years of age: For subjects ≥ 50 kg, a starting dose of 0.5 mg once daily is recommended. This dosage can be individually adjusted by increments of 0.5 mg once daily not more frequently than every other day, if needed. The optimum dose is 1 mg once daily for most patients. Some patients, however, may benefit from 0.5 mg once daily while others may require 1.5 mg once daily. For subjects < 50 kg, a starting dose of 0.25 mg once daily is recommended. This dosage can be individually adjusted by increments of 0.25 mg once daily not more frequently than every other day, if needed. The optimum dose is 0.5 mg once daily for most patients. Some patients, however, may benefit from 0.25 mg once daily while others may require 0.75 mg once daily.

As with all symptomatic treatments, the continued use of Rischotic® must be evaluated and justified on an ongoing basis.

Rischotic® is not recommended in children less than 5 years of age, as there is no experience in children less than 5 years of age with this disorder.

Renal and hepatic impairment

Patients with renal impairment have less ability to eliminate the active antipsychotic fraction than in adults with normal renal function. Patients with impaired hepatic function have increases in plasma concentration of the free fraction of Rischotic®.

Irrespective of the indication, starting and consecutive dosing should be halved, and dose titration should be slower for patients with renal or hepatic impairment.

Rischotic® should be used with caution in these groups of patients.

Method of administration

Rischotic® is for oral use. Food does not affect the absorption of Rischotic®.

Upon discontinuation, gradual withdrawal is advised. Acute withdrawal symptoms, including nausea, vomiting, sweating, and insomnia have very rarely been described after abrupt cessation of high doses of antipsychotic medicines. Recurrence of psychotic symptoms may also occur, and the emergence of involuntary movement disorders (such as akathisia, dystonia and dyskinesia) has been reported.

Switching from other antipsychotics

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

OVERDOSAGE

In general, reported signs and symptoms have been those resulting from an exaggeration of the known pharmacological effects of Risperidone. 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 Risperidone and paroxetine.

In case of acute overdose, the possibility of multiple drug involvement should be considered. 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 only when drug intake was less than one hour before. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias.

There is no specific antidote to Risperidone. 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.

STORAGE CONDITIONS

Store below 30°C.

Keep in original pack in intact conditions.

Date of revision: february 2014.

This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you
- Follow strictly the doctor's prescription, the method of use, and the instructions of the pharmacist who sold the medicament
- The doctor and the pharmacist are experts in medicine, its benefits and risks
- Do not by yourself interrupt the period of treatment prescribed for you
- Do not repeat the same prescription without consulting your doctor
- Medicament: keep out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists

Benta S.A.L
Dbayeh - Lebanon

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