Rischotic® OD

Risperidone

FORMS AND PRESENTATION
Rischotic® OD 0.5: Orally disintegrating tablets: Box of 30.
Rischotic® OD 1: Orally disintegrating tablets: Box of 30.
Rischotic® OD 2: Orally disintegrating tablets: Box of 30.
Rischotic® OD 3: Orally disintegrating tablets: Box of 30.
Rischotic® OD 4: Orally disintegrating tablets: Box of 30.

COMPOSITION
Rischotic® OD 0.5: Each orally disintegrating tablet contains Risperidone 0.5mg.
Rischotic® OD 1: Each orally disintegrating tablet contains Risperidone 1mg.
Rischotic® OD 2: Each orally disintegrating tablet contains Risperidone 2mg.
Rischotic® OD 3: Each orally disintegrating tablet contains Risperidone 3mg.
Rischotic® OD 4: Each orally disintegrating tablet contains Risperidone 4mg.
Excipients: magnesium aluminometasilicate, aspartame, colloidal silicon dioxide, hydroxypropyl cellulose, sodium stearyl fumarate, methacrylate copolymer, talc, sodium lauryl sulfate, acesulfame potassium, mannitol, sodium chloride, peppermint flavor, yellow iron oxide (Rischotic® OD 0.5), FD&C blue (Rischotic® OD 2), FD&C yellow (Rischotic® OD 3), red iron oxide (Rischotic® OD 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 serotoninergic 5-HT2 and dopaminergic D2 receptors. Risperidone binds also to alpha1-adrenergic receptors, and, with lower affinity, to H1-histaminergic and alpha2-adrenergic receptors. Risperidone has no affinity for cholinergic receptors. Although Risperidone is a potent D2 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 effect 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 relative oral bioavailability of Risperidone from a tablet is 94% compared with a solution.
Distribution
Risperidone is rapidly distributed. 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.
Another metabolic pathway of Risperidone is N-dealkylation.
Elimination
One week after administration, 70% of the dose is excreted in the urine and 14% in the feces. After oral administration, 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® OD 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.

CONTRAINDICATIONS
- Hypersensitivity to Risperidone or to any of the excipients.

PRECAUTIONS
Elderly patients with dementia
- Overall mortality: Elderly patients with dementia treated with atypical antipsychotics have an increased mortality compared to placebo in a meta-analysis of 17 controlled trials of atypical antipsychotics, including Risperidone.
Cerebrovascular events, including stroke, in elderly patients with dementia-related psychosis: Risperidone® OD is not approved for use in patients with dementia-related psychosis
Neuroleptic Malignant Syndrome: Manage with immediate discontinuation of Risperidone® OD and close monitoring.
• Tardive dyskinesia: Consider discontinuing Risperidone® OD if clinically indicated.
• Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/ cerebrovascular risk. These metabolic changes include hyperglycemia, dyslipidemia, and weight gain.
o Hyperglycemia and Diabetes Mellitus: Monitor patients for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Monitor glucose regularly in patients with diabetes or at risk for diabetes. (5.5)
o Weight Gain: Significant weight gain has been reported. Monitor weight gain.
• Hyperprolactinemia: Prolactin elevations occur and persist during chronic administration.
• Orthostatic hypotension: For patients at risk, consider a lower starting dose and slower titration.
• Leukopenia, Neutropenia, and Agranulocytosis: Perform complete blood counts in patients with a history of clinically significant low white blood cell count (WBC). Consider discontinuing Risperidone® OD if a clinically significant decline in WBC occurs in the absence of other causative factors.
• Potential for cognitive and motor impairment: Use caution when operating machinery.
• Seizures: Use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold.

Excipients
The orodispersible tablets contain aspartame. Aspartame is a source of phenylalanine which may be harmful for people with phenylketonuria.

PREGNANCY AND LACTATION
There are no adequate data from the use of Risperidone in pregnant women. Neonates exposed to antipsychotics 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. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Risperidone was not teratogenic in animal studies but other types of reproductive toxicity were seen. Risperidone should not be used during pregnancy unless clearly necessary. If discontinuation during pregnancy is necessary, it should not be done abruptly.
It has been demonstrated that Risperidone and 9-hydroxy-risperidone are excreted in human breast milk in small quantities. There are no data available on adverse reactions in breast-feeding infants. Therefore, the advantage of breastfeeding 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 and class III antiarrhythmics tricyclic antidepressant, tetracyclic antidepressants, 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.
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.
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
- 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.
- Verapamil, an inhibitor of CYP 3A4 and P-gp, increases the plasma concentration of Risperidone.
- Phenothiazines, tricyclic antidepressants, and some beta-blockers may increase the plasma concentrations of Risperidone but not those of 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.
- 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 Effect
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).
- 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, bradykinesia, hypokinesia, muscle rigidity), headache (very common); akathisia (restlessness, hyperkinesia, and restless leg syndrome), dizziness, tremor, dystonia, somnolence, sedation, lethargy (common); unresponsive to stimuli, loss of consciousness, syncope, hypersomnia, balance disorder, tardive dyskinesia, speech disorder, Neuroleptic Malignant Syndrome, diabetic coma,(rare).
- Eye disorders: Blurred vision (common); conjunctivitis, ocular hyperemia, eye discharge, eye swelling, dry eye, increased lacrimation, photophobia (uncommon); reduced visual acuity, glaucoma (rare).
- Ear and labyrinth disorders: Ear pain, tinnitus (uncommon).
- Respiratory, thoracic and mediastinal disorders: Dyspnea, epistaxis, cough, congestion, pharyngo-laryngeal pain (common); wheezing, pneumonia aspiration, rales, 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, (uncommon); intestinal obstruction, pancreatitis, lip swelling, (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, pruritus, skin discoloration, alopecia, seborrheic dermatitis, dry skin, hyperkeratosis (uncommon).
- Musculoskeletal and connective tissue disorders: Arthralgia, back pain, pain in extremity (common); muscular weakness, myalgia, neck pain, joint swelling, 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).
- Infections and infestations: Pneumonia, bronchitis, upper respiratory tract infection, urinary tract infection (common); sinusitis, viral infection, tonsillitis, cellulitis, otitis media, eye infection, respiratory tract infection.
- Vascular disorders: Hypotension, orthostatic hypotension, flushing (uncommon).
- 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).
- Psychiatric disorders: Insomnia (very common); anxiety, agitation, sleep disorder (common); confusional state, mania, decreased libido, listless, nervousness (uncommon).

DOSAGE AND ADMINISTRATION
Schizophrenia
- Adults: Rischotic® OD may be given once daily or twice daily.
Patients should start with 2 mg/day Rischotic® OD. The dosage may be increased on the second day to 4 mg. Most patients will benefit from daily doses between 4 and 6 mg. 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® OD 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® OD should be administered on a once daily schedule, starting with 2 mg Rischotic® OD. Dosage adjustments, if indicated, should occur at intervals of not less than 24 hours and in dosage increments of 1 mg per day. Rischotic® OD 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 Rischotic® OD have not been investigated in patients with manic episodes.
- 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® OD 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® OD should not be used more than 6 weeks in patients with persistent aggression in Alzheimer's dementia.
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.
Rischotic® OD 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 and have increases in plasma concentration of the free fraction of Rischotic® OD.
Irrespective of the indication, starting and consecutive dosing should be halved, and dose titration should be slower for patients with renal or hepatic impairment.
Method of administration
Rischotic® OD is for oral use. Food does not affect the absorption of Rischotic® OD.
Place the tablet on the tongue. The tablet will begin disintegrating within seconds. Water may be used if desired. No attempt should be made to divide the tablet.
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® OD therapy is initiated is recommended. Also, if medically appropriate, when switching patients from depot antipsychotics, initiate Rischotic® OD therapy in place of the next scheduled injection. The need for continuing existing anti-Parkinson medicines should be re-evaluated periodically.

OVERDOSAGE
In general, the reported signs and symptoms may include drowsiness and sedation, tachycardia and hypotension, extrapyramidal symptoms, QT-prolongation , convulsions, Torsade de Pointes .
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.

STORAGE CONDITIONS
Store below 30°C.
Keep in original pack in intact conditions.

Date of revision: April 2019.

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

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