xxxxxxxxxx-5253

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory

RESPIDON 1 MG TABLETS
RESPIDON 2 MG TABLETS
RESPIDON 3 MG TABLETS

(Risperidone Tablets 1mg/2mg/3mg)

BRAND OR PRODUCT NAME

RESPIDON 1 MG TABLETS
RESPIDON 2 MG TABLETS
RESPIDON 3 MG TABLETS

NAME AND STRENGTH OF ACTIVE SUBSTANCE(S)

RESPIDON 1 MG TABLETS
Each film coated tablet contains:
Risperidone……1 mg
RESPIDON 2 MG TABLETS
Each film coated tablet contains:
Risperidone……2 mg
RESPIDON 3 MG TABLETS
Each film coated tablet contains:
Risperidone……3 mg

PRODUCT DESCRIPTION

RESPIDON 1 MG TABLETS:
White, biconvex, oblong film coated tablets with break line on one side.
RESPIDON 2 MG TABLETS:
Pale orange, biconvex, oblong film coated tablets with break line on one side.
RESPIDON 3 MG TABLETS
Light yellow, biconvex, oblong film coated tablets with break line on one side.

Pharmacodynamic:

Chemically Risperidone is benzisoxazole derivatives. It is novel class of antipsychotic agent.
Mechanism of action:
Risperidone is a selective monoaminergic antagonist having high affinity for both seratonergic 5-HT2 and dopaminergic D2 receptors. Risperidone also binds with the alpha1-adrenergic receptors, H1-histaminergic and alpha2-adrenergic receptors. Risperidone has no affinity for cholinergic receptors. Risperidone improves the positive symptoms of schizophrenia because it is potent D2 antagonist. As compared to classical neuroleptics, risperidone can cause less depression of motor activity and induction of catalepsy. Due to its balanced central serotonin and dopamine antagonistic property it may reduce the tendency to cause extra pyramidal side-effects, and extend the therapeutic activity to the negative and affective symptoms of schizophrenia.

Pharmacokinetic:

Absorption:
Risperidone is completely absorbed after oral administration. Peak plasma concentration reaches within 1 to 2 hours. Absorption of Risperidone in stomach cannot be affected by food. The study related to effect of food particles in the mouth on absorption has not been performed.
Metabolism:
Risperidone get metabolized by CYP 2D6 to its hydroxyl metabolite that is 9-hydroxy Risperidone having similar pharmacological effect as that of Risperidone. Then it can lead to debrisoquine-type genetic polymorphism not affects antipsychotic fraction because it consists of Risperidone and its active metabolite that is 9-hydroxy Risperidone.
Excretion:
After oral administration, the elimination half-life of active antipsychotic fraction is 24 hours. A single dose study indicates that in case of elderly patient and patients with renal insufficiency, higher active plasma concentration and slower elimination of risperidone can occur. In case of patient with liver insufficiency Risperidone plasma concentration were normal.

Indication:

RESPIDON tablets are indicated for the treatment of acute and chronic schizophrenic psychoses. It is indicated in other psychotic conditions, wherein positive symptoms (such as hallucinations, delusions, thought disturbances, hostility, and suspiciousness) and/or negative symptoms (such as blunted affect, emotional and social withdrawal, poverty of speech) are prominent. RESPIDON tablets also alleviate affective symptoms (such as depression, guilt feelings and anxiety) associated with schizophrenia. RESPIDON tablets are also effective in maintaining the clinical improvement during continuation therapy in patients who have shown initial treatment response.

Recommended dosage:

Schizophrenia
Switching from other antipsychotics: When initiating therapy with RESPIDON tablets, gradual discontinuation of the previous treatment is recommended where medically appropriate. The need for continuing existing antiparkinson medication should be re-evaluated periodically.
Adults: RESPIDON treatment should be initiated in patients whether acute or chronic at a dose of 2mg once daily. On the second day the dosage may be increased to 4mg/day. For the first episode patient's lower dose may be useful but after that dosage can be individualized depending on the symptoms. Daily dose of 4 and 6 mg will benefit most of the patients, however at lower doses optimal response may be obtained.
The daily doses of RESPIDON above 10mg, is not beneficial because it does not provide additional efficacy to that of lower doses and the risk of extrapyramidal symptoms may be more. If it shows additional efficacy and lower side effects, for that patient doses above 10mg/day can be used. The daily dose above 16 mg should not be used for safety purpose. Elderly: The usual starting dose recommended in the elderly is 0.5 mg twice daily. This can be increased up to 1-2 twice daily.
Children: Treatment of RESPIDON in schizophrenia for children less than 15 years of age has not been formally evaluated.
Renal and liver disease: The daily effective starting dose of RESPIDON 0.5 mg twice daily is recommended and it can be increased up to 1 to 2 mg twice daily as per the individual. In case of patients with renal and liver disease RESPIDON should be used with greater caution

Method of administration
Oral use:
RESPIDON tablets should be swallowed with a drink of water, with or without food. They should not be chewed or crushed.

Contraindications:

Risperidone is contraindicated in patients with a known hypersensitivity to RESPIDON or any other ingredients of the RESPIDON tablet. It is also contraindicated in patient with coma caused by CNS depressents, bone-marrow depression and avoided in phaeochromocytoma.

Warning and precaution:

Hyperglycemia and Diabetes Mellitus
Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. 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 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 hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.
Risperidone is not recommended for the treatment of behavioral symptoms of: Dementia due to an increased risk of cerebrovascular adverse events such as cerebrovascular accidents and transient ischaemic attacks. In patients with a history of dementia, treatment of acute psychoses should be limited to short term only and it should be under specialist advice.
Data from randomized clinical trials conducted in elderly > 65 years patients with dementia indicate that Risperidone treatment shows an approximately 3-fold increased risk of cerebrovascular adverse events (including cerebrovascular accidents and transient ischaemic attacks), compared with placebo. Cerebrovascular adverse events 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).
Before treating any patient with a previous history of cerebrovascular accidents and transient ischaemic attacks, physicians should consider carefully the risk of cerebrovascular adverse events with Risperidone (given the observations in elderly patients with dementia detailed above). Other risk factors should also be considered for cerebrovascular disease including hypertension, diabetes, current smoking, atrial fibrillation, etc.
Orthostatic hypotension:
Risperidone causes orthostatic hypotension during the initial treatment period because of its alpha blocking activity. And dose can be reduced if hypotension occurs.
Cardiovascular disease:
In case of patients with known cardiovascular disease including those that are associated with prolongation of QT interval, Risperidone can be used with greater caution and the dose can be reduced. Risperidone was not associated with an increase in QTc intervals. Similar to that of antipsychotic greater caution can be taken for prescribing the medications which known to increase QT interval.
Sedation:
For getting further sedation another additional drug such as Benzodiazepines should be administered instead of increasing the dose of Risperidone.
Tardive dyskinesia:
The drugs having dopamine receptor antagonistic properties are associated with rhythmical involuntary movements generally of the tongue and/or face, which is called tardive dyskinesia. The occurrence of extrapyramidal symptoms is the risk factor for tardive dyskinesia. The antipsychotic drugs should be discontinued whenever these symptoms appear.
Neuroleptic malignant syndrome:
Hyperthermia, muscle rigidity, autonomic instability, altered consciousness and increased CPK levels, has been reported to occur with neuroleptics, which is neuroleptic malignant syndrome. For these symptoms Risperidone and all the antipsychotic should be discontinued.
Renal and hepatic failure:
It should be recommended for starting as well as for subsequent increment dose of Risperidone for geriatric patients and for patients with renal and hepatic failure should be halve.
Parkinson's disease:
During recommendation of Risperidone tablet greater care should be taken for prescribing to patients with Parkinson's disease because theoretically it may deteriorate the disease condition.
Seizures:
Seizure threshold can be lowered by classical neuroleptics; therefore caution can be taken for treating epileptic patients.
Weight gain:
Similar as that for antipsychotics weight gain is associated with Risperidone.
Withdrawal symptoms:
After the high dose treatment with antipsychotic drugs, it is associated with acute withdrawal symptoms that include nausea, vomiting, sweating and insomnia. Other withdrawal symptoms include recurrence of psychotic symptoms, involuntary movement disorders such as akathisia, dystonia and dyskinesia. Therefore gradual withdrawal is advisable.
Children below 15 years age:
Risperidone treatment in schizophrenic children having age less than 15 years has not been formally evaluated.
Intraoperative Floppy Iris Syndrome:
Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in patients treated with medicines with alpha 1a-adrenergic antagonist effect, including risperidone. IFIS may increase the risk of eye complications during and after the operation. Current or past use of medicines with alpha 1a-adrenergic antagonist effect should be made known to the ophthalmic surgeon in advance of surgery. The potential benefit of stopping alpha 1 blocking therapy prior to cataract surgery has not been established and must be weighed against the risk of stopping the antipsychotic therapy.

Drug Interaction:

Alcohol:
The possible drug interactions of Risperidone with other drugs have not been systematically evaluated. Since Risperidone has CNS effects, greater care should be taken in combination with other CNS drugs including alcohol.
Levodopa and other dopamine agonists:
The effects of levodopa and other dopamine agonists may antagonize by Risperidone.
Carbamazepine:
The plasma level of antipsychotic fraction of Risperidone has been shown to decrease by carbamazepine. Similar can happen with the drug that stimulates the metabolizing enzymes in the liver. On concomitant use of carbamazepine and other hepatic enzyme inducing drugs, the dose of Risperidone should be evaluated and increased if necessary. Conversely, on discontinuation of such drugs, the dose of Risperidone should be re-evaluated and increased if necessary.
Phenothiazines, tricyclic antidepressants and some beta blockers:
On concomitant use of phenothiazine, tricyclic antidepressants and some beta blockers with Risperidone causes increase in the plasma concentration of Risperidone but not of the antipsychotic fraction. Fluoxetine may also increase the plasma concentration of Risperidone but not as that of the antipsychotic fraction. The dose of the Risperidone should be reduced when concomitantly used with fluoxetine. Haloperidol may also cause same type of drug interaction.
Erythromycin
Erythromycin, a CYP 3A4 inhibitor, does not change the pharmacokinetics of risperidone and the active antipsychotic fraction.
Cholinesterase Inhibitor
The cholinesterase inhibitor galantamine does not show a clinically relevant effect on the pharmacokinetics of risperidone and the active antipsychotic fraction.
Valproate
Risperdal does not show a clinically relevant effect on the pharmacokinetics of valproate. However, it has been reported that there was a 20% increase in valproate peak plasma concentration (Cmax) after concomitant administration of risperidone.
Lithium
In patients on long-term lithium and older/typical neuroleptic therapy, no significant change occurred in the pharmacokinetics of lithium after substitution of the concomitant neuroleptic with risperidone.
Digoxin
Risperidone did not show a clinically relevant effect on the pharmacokinetics of digoxin.
Highly protein bound drugs:
Administration of highly protein bound drugs with Risperidone cannot cause displacement of either drug significantly.
Food:
Risperidone absorption in stomach cannot be affected by food.

Pregnancy and lactation:

Pregnancy:
Reproductive study on experimental animals did not show any significant reproductive toxicity but some of the CNS and prolactin related effects were observed such as mating and nursing behaviour and delayed oestrus. Risperidone is not associated with any teratogenic effect. No any significant data is available for use of Risperidone in human pregnancy. Therefore Risperidone should only be used during pregnancy if the benefits outweigh the risks.
Nursing Mother:
Risperidone and 9-hydroxy Risperidone are observed to be excreted in human breast milk, also observed from animal study indicates that woman receiving Risperidone should not breast feed.

Adverse Effects / Undesirable Effects

Infections and infestations: Nasopharyngitis, upper respiratory tract infection, Sinusitis, Urinary tract infection, pneumonia, cellulitis, rhinitis, influenza, Ear infection, Viral infection, Pharyngitis, Tonsillitis, Bronchitis, Eye infection, Localised infection, Cystitis, Otitis media, Onychomycosis, Acarodermatitis, Bronchopneumonia, respiratory tract infection, Tracheobronchitis, Otitis media chronic.
Blood and Lymphatic System Disorders: Anemia, Granulocytopenia, Thrombocytopeniaa,
Agranulocytosis
Immune System Disorders: Hypersensitivity, drug Hypersensitivity, Anaphylactic reaction
Endocrine Disorders: Hyperprolactinaemia, Inappropriate anti-diuretic hormone secretion
Metabolism and nutritional disorder: decreased appetite, Polydipsia, Anorexia, Diabetic ketoacidosis, increased appetite, Water intoxication
Psychiatric Disorders: Insomnia, Anxiety, Nervousness, confusional state, middle insomnia, Listless, Agitation, Blunted affect, Sleep disorder, Libido decreased, Anorgasmia, Mania
Nervous System Disorders: Parkinsonism*, Akathisia*, Dizziness, Somnolence, Sedation, Tremor*, Dystonia*, Dizziness postural, Dyskinesia*, Syncope, Lethargy, transient ischemic attack, depressed level of consciousness, drooling, cerebrovascular accident, headache, dysarthria, disturbance in attention, balance disorder, hypersomnia, Unresponsive to stimuli, Coordination abnormal, Loss of consciousness, Speech disorder, Hypoesthesia, Movement disorder, Tardive dyskinesia, Cerebral ischaemia, Cerebrovascular disorder, Neuroleptic malignant syndrome, Diabetic coma
Eye Disorders: Vision blurred, Conjunctivitis, Ocular hyperaemia, Eye discharge, Eye rolling, Eyelid edema, Eye swelling, Eyelid margin crusting, .Dry eye, Lacrimation increased, Photophobia, Glaucoma, Visual acuity reduced, Floppy Iris Syndrome (Intraoperative).
Ear and Labyrinth Disorders: Ear pain, tinnitus
Cardiac Disorders: Tachycardia, palpitation, Sinus bradycardia, Sinus tachycardia, Atrioventricular block first degree, Bundle branch block left, Bundle branch block right, Atrioventricular block, Atrial fibrillation
Vascular Disorders: Orthostatic hypotension, hypotension, Flushing,
Respiratory, Thoracic and Mediastinal Disorders: Nasal congestion, Dysponea, Epistaxis, sinus congestion, cough, Rhinorrhoe, pharyngolaryngeal pain, pulmonary congestion, Wheezing, Pneumonia aspiration, Dysphonia, productive cough, Respiratory tract congestion, Rales, Respiratory disorder, Nasal edema, Hyperventilation, Sleep apnea syndrome
Gastrointestinal Disorders: Nausea, Constipation, Dyspepsia, Vomiting, Diarrhea, Salivary hypersecretion, Dry mouth, Abdominal discomfort, Abdominal pain, Stomach discomfort, Abdominal pain upper, Dysphagia, faecaloma, Fecal incontinence, Gastritis, Lip swelling, Cheilitis, Aptyalism, Intestinal obstruction, Pancreatitis,
Skin and Subcutaneous Tissue Disorders: Rash, Dry skin, Dandruff, Seborrheic dermatitis, Hyperkeratosis, erythema, pruritus, acne, Skin discoloration, Skin lesion, Skin disorder, Rash erythematous, Rash papular, Rash generalised, Rash maculo-papular, Angioedemab, Alopecia
Musculoskeletal and Connective Tissue Disorders: Back pain, Arthralgia, Pain in extremity, Postural abnormal, joint swelling, myalgia, neck pain, musculoskeletal chest pain, Joint stiffness, Muscular weakness, Rhabdomyolysis
Renal and Urinary Disorders: Urinary incontinence, enuresis, urinary incontinence, pollakiuria, Dysuria
Reproductive System and Breast Disorders: Ejaculation failure, galactorrhea, menstruation irregular, Amenorrhea, Gynaecomastla, Vaginal discharge, Erectile dysfunction, Ejaculation disorder, Menstrual disorder, Breast enlargement, sexual dysfunction, Retrograde ejaculation, Priapism,
General Disorders: Fatigue, Chest pain, Asthenia, pyrexia, Oedema peripheral, gait disturbance, pitting oedema, feeling abnormal, sluggishness, chest discomfort, Thirst, Influenza-like illness, Edema, Malaise, Face edema, Discomfort, Generalised edema, Chills, Peripheral coldness, Drug withdrawal syndrome, Hypothermia, Adverse drug reaction
Investigations: Blood creatine phosphokinase increased, Heart rate increased, Body temperature increased, weight increased, blood prolactin increased, Alanine aminotransferase increased, Electrocardiogram abnormal, Eosinophil count increased, Aspartate aminotransferase increased, White blood cell count decreased, Blood glucose increased, Hemoglobin decreased, Hematocrit decreased, Body temperature decreased, Blood pressure decreased, Transaminases increased, Elec~rocardiogram QT prolonged[c]
Hepatobiliary Disorders: Jaundice
*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. Dyskinesia includes dyskinesia, muscle twitching, chorea, and choreoathetosis.
[a]Search terms included Thrombocytopenia, Platelet count decreased, Plateletcrit decreased, Platelet production decreased.
[b]Search terms included Angioneurotic oedema, C1 esterase deficiency acquired, Circumoral oedema, Eyelid edema, Face edema, Hereditary angioedema, Laryngeal oedema, Laryngotracheal oedema, Oculorespiratory syndrome, Oedema mouth, Periorbital edema, Small bowel angioedema, Tongue oedema.
[c]Search terms included Electrocardiogram QT corrected interval prolonged, Electrocardiogram QT interval abnormal, Electrocardiogram QT prolonged, Long QT syndrome, Long QT syndrome congenital.
Effect on ability to drive and use machines:
Risperidone may impair mental alertness the abilities required to perform skills tasks such as driving a car or operating machinery, patients such be warned accordingly. Risperidone should not be administered in patients who drive or operate machinery.

Overdosage:

Symptoms and signs:
The symptoms and signs from overdose of Risperidone are due to an exaggeration of the drug's known pharmacological effects that includes drowsiness and sedation, tachycardia and hypotension, and extrapyramidal symptoms. Overdose of Risperidone can rarely cause QT prolongation. Possibility of multiple drug involvement should be considered during acute over dosage.
Treatment:
There are no specific antidotes to Risperidone. Therefore appropriate supportive measures should be considered. Establish and maintain clear airway. Adequate oxygenation and ventilation should be instituted. Administration of activated charcoal with a laxative and gastric lavage after intubation if the patient is unconscious should be considered. For detection of any possible arrhythmias cardiological monitoring and electrocardiographic monitoring should commenced immediately. Intravenous fluids and/or sympathomimetic agents should be used for the treatment of hypotension and circulatory collapse. For severe extrapyramidal symptoms anticholinergic should be used. Close medical supervision and monitoring should continue until the patient recovers.

Storage

Store below 30°C.

Presentation

RESPIDON 1mg, 2mg and 3mg tablets are available in blister strip of 1x10, 2x10, 6x10 and 10x10 tablets. Not all presentations or all pack sizes may be marketed.

DATE OF REVISION OF PACKAGE INSERT

13th May 2015

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.