RISPONZ RISPONZ

Rx **RISPERIDONE**

RISPONZ 1
RISPONZ 2
RISPONZ 3
1 mg, 2mg & 3mg Film-Coated Tablet

Antipsychotic

FORMULATION
Each film-coated tablet contains
Risperidone (Risponz 1) …….. 1mg
Risperidone (Risponz 2) …….. 2mg
Risperidone (Risponz 3) …….. 3mg

PRODUCT DESCRIPTION
Risperidone tablet contain Risperidone as an active ingredient which is a psychotropic agent belonging to the chemical class of benzisoxazole derivatives.
The chemical designation is 3-[2-[4–(6-benzisoxazol-3-yl)- 1-piperidinyl]ethyl-6,7,8,9-etrahydro–2-methyl-4H-pyrido(1,2- a)Pyrimidin-4–one. Its molecular formula is $C_{22}H_{27}FN_4O_2$ and its molecular weight is 410.49.
Risperidone is a white to slightly beige powder. It is practically insoluble in water, freely soluble in methylene chloride, and soluble in methanol and 0.1 N HCl.

INDICATIONS
For the treatment of schizophrenia and other psychoses and in the short-term treatment of acute manic or mixed episodes associated with bipolar disorder, and for the treatment of irritability associated with autistic disorder.

CLINICAL PHARMACOLOGY
Pharmacodynamic:
Risperidone (Risponz) is an antipsychotic of the bensisoxazol derivatives, It is a selective monoaminergic antagonist. Risperidone (Risponz) has affinity for serotonin-5-HT2. dopamine-D2, H1-histaminic, alpha 1 and alpha 2-adrenergic receptors. Risperidone (Risponz) has no affinity for cholinergic receptors. It is a potent D2-antagonist.

Pharmacokinetics:
Risperidone (Risponz) is completely absorbed after oral administration. Peak plasma concentrations are attained within 1 to 2 hours. Food does not affect the absorption of Risperidone.
Risperidone is metabolized by cytochrome P-450 11D6 to 9-hydroxy-Risperidone which has a similar pharmacological activity to Risperidone. Risperidone and 9-hydroxy-risperidone form the active antipsychotic fraction.
After oral administration to psychotic patients, Risperidone's half-life is about 3 hours. The elimination half-life of 9-hydroxy-risperidone and the active antipsychotic fraction is 24 hours.
Following 6 mg or 8 mg once daily, peak levels of the active moiety were about 30% higher and trough levels about 30% lower than the peaks and troughs following 3 and 4mg twice daily.
Steady state is reached within 1 day for Risperidone (Risponz) in most patients and 4-5 days for 9-hydroxyrisperidone. Risperidone plasma concentration is dose—proportional within the therapeutic dose-range.
Risperidone (Risponz) is bound to albumin and alpha1-acid glycoprotein. Plasma protein binding of Risperidone is 88% and 77% for 9-hydroxy- risperidone. One week after administration, 70% of the dose is excreted in the urine and 14% in the faeces. In urine, Risperidone and 9-hydroxy-risperidone represent 35-45% of the dose.
Risperidone (Risponz) showed higher active plasma concentrations and slower elimination in the elderly and in patients with renal insufficiency. The plasma concentrations of Risperidone (Risponz) were normal in patients with liver insufficiency.
The pharmacokinetics of Risperidone, 9-hydroxy-risperidone and the active moiety in children are similarto those in adults.

DOSAGE AND MODE/ROUTE OF ADMINISTRATION
Risperidone (Risponz) is a benzisoxazole antipsychotic reported to be an antagonist at dopamine D2 and serotonin (5-HT2), adrenergic (α1and α2), and histamine (H1) receptors. It is described as an atypical antipsychotic. It is given by mouth for the treatment of schizophrenia and other psychoses.
Risperidone (Risponz) may be given in 1 or 2 devided doses daily. The usual initial daily dose of Risperidone (Risponz) is 2 mg on the first day, 4 mg on second day and 6 mg on the third day. Further dosage adjustment may be needed and should generally be made at interval of not less than one week; usual maintenance doses are 4 to 8 mg daily. Extra pyramidal symptoms may be more likely with doses above 10 mg daily. The maximum recommended dose is 16 mg daily.
An initial dose of 0.5 mg twice daily slowly increased in steps of 0.5 mg twice daily to a dose of 1 to 2 mg twice daily suggested for the elderly and for patient with renal or hepatic impairment.
Schizophrenia: The use of Risperidone(Risponz) for the management of schizophrenia has been reviewed. Features for which Risperidone (Risponz) has bee promoted have included a relatively low incidence of extra pyramidal effect and efficacy against both positive and negative symptoms of schizophrenia. Most studies have compared Risperidone with haloperidol but, of these, some of the major studies have been criticized for potential methodological flaws and it is difficult to determine any difference in efficacy including effect on negative symptoms. The production of extra pyramidal effects appears to be dose dependent Risperidone (Risponz). Overall the incidence for Risperidone (Risponz) appears to be similar to that for placebo but at doses of more than 10 mg it appears to approach that associated with haloperidol. In the few comparative studies with other atypical antipsychotics Risperidone (Risponz) has appeared to be of similar efficacy to clozapine.
Dementia: Risperidone (Risponz) has been used for the management of behavioural disturbances in patients with dementia. Although there have been anecdotal reports of efficacy in patient with Lowy body dementia other reports suggest that these patients are likely to be just as sensitive to Risperidone (Risponz) as to standard antipsychotic

CONTRAINDICATION
Risperidone (Risponz) is contra-indicated in patients with known sensitivity to the medicine. Safety of Risperidone (Risponz) in pregnancy or lactating women has not been established. Risperidone (Risponz) and 9-hydroxy-risperidone are excreted in human breast milk. Therefore, women receiving Risperidone (Risponz) should not breastfeed.
Conduct and 'other disruptive behavioural disorders children: Not for children under 5 years as efficacy and safety in children under the age of 5 years have not been demonstrated.

ADVERSE DRUG REACTIONS
In some instances it has been difficult to differentiate adverse events from symptoms of the underlying psychosis. The most frequent side-effects observed with Risperidone (Risponz) are: insomnia, agitation, extra pyramidal disorder, anxiety headache. Sedation has been reported more frequently in children and adolescents than in adults.
Less commonly observed are: somnolence, fatigue, dizziness, impaired concentration, constipation, dyspepsia. Nausea, vomiting, abdominal pain, weight gain, blurred vision, priapism, erectile dysfunction, ejaculatory dysfunction. orgastic dysfunction, urinary incontinence, rhinitis, rash and other reactions reactions have been observed.
The following dose dependent extra pyramidal symptoms have been observed: tremor, rigidity, hypersalivation, bradykinesia, oculogyric crisis, akathisia (hyperkinesia) and acute dystonia, hypokinesia. These are usually mild and reversible upon dose reduction and/or administration of anti-Parkinson medication, if necessary.
Tardive dyskinesia (TD), a syndrome consisting of potentially irreversible, involuntary dyskinetic movements may develop in patients treated with conventional neuroleptics. Although this syndrome of TD appears to be most prevalent in the elderly especially elderly females, it is impossible to predict at the onset of treatment which patients are likely to develop TD.
It has been suggested that the occurrence of Parkinsonian side- effects is a predictor for the development of TD. The risk of developing TD and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of the antipsychotic administered to the patient increase, however, the syndrome can develop, although less commonly, after relatively brief periods of treatment at low doses. There is no known treatment for an established case of TD. The syndrome may remit partially or completely if the antipsychotic medicine treatment is withdrawn.
The antipsychotic drug treatment itself however, may suppress the signs and symptoms of TD, thereby masking the underlying process. The effect of symptom suppression upon the long-term course of TD is unknown. In view of these considerations, Risperidone (Risponz) should be prescribed in a manner that is most likely to minimize the risk of TD. As with any antipsychotic medicine, Risperidone (Risponz) should be reserved for patients who appear to be obtaining substantial benefit from the medicine. In such patients the smallest dose and the shortest duration of treatment should be sought. The benefit for continued treatment should be reassessed periodically. If signs and symptoms of TD appear in a patient on antipsychotics, medicine discontinuation should be considered. However, some patients may require treatment despite the presence of this syndrome.
Neuroleptic Malignant Syndrome (NMS) is a potentially fatal symptom complex that has been reported in association with antipsychotic medicines, including Risperidone (Risponz). Clinical manifestations of NMS are hyperthermia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, cardiac arrhythmias and diaphoresis). Additional signs may include elevated creatine phosphokinase (CPK) levels, myoglobinuria (rhabdomyolysis), and acute renal failure.
In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illnesses (e.g. pneumonia, systemic infection, etc.) and untreated or inadequately treated extra pyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, medicine fever and primary central nervous system pathology.
The management of NMS should include
1. Immediate discontinuation of all antipsychotic medicines and other drugs not essential to concurrent therapy;
2. Intensive symptomatic treatment and medical monitoring; and
3. Treatment of any concomitant serious medical problems for which specific treatments are available.
There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.
If a patient requires antipsychotic medicine treatment after recovery from NMS, the potential reintroduction of medicine therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.
Classical neuroleptics are known to lower the seizure threshold. Seizures have been reported alter treatment with Risperidone (Risponz). Caution is recommended when treating patients with epilepsy.
(Orthostatic) hypotension and (reflex) tachycardia or hypertensions have been observed. A mild fall in neutrophil and/or thrombocytes count has been reported.
Risperidone (Risponz) can induce a dose-dependent increase in plasma prolactin concentration. Possible associated manifestations are: galactorrhoea. gynaecomastia, disturbances of the menstrual cycle and amenorrhoea, Premenopausal women who develop secondary amenorrhea of greater than six months duration should receive appropriate preventative therapy to avoid hypo oestrogenic bone loss.
Cerebrovascular accidents have been observed during treatment with Risperidone (Risponz).
Water intoxication, either due to polydipsia or the syndrome of inappropriate secretion of the antidiuretic hormone (SIADH), and body temperature disregulation, have been reported.

PRECAUTIONS
Risperidone (Risponz) may impair mental alertness. Therefore patients should be advised not to drive or operate machinery until their individual susceptibility is known.
It is recommended to have both the starting dose and the subsequent dose increments in geriatric patients and patients with renal or liver insufficiency.
Due to the alpha-blocking activity of Risperidone (Risponz), (orthostatic) hypotension can occur, especially during the initial dose-titration period. Risperidone (Risponz) should be used with caution in patients with known cardiovascular disease, and the dosage should be gradually titrated as recommended. A dose reduction should be considered if hypotension occurs.
Caution should be used when prescribing Risperidone (Risponz) to patients with Parkinson disease since, theoretically, it might cause a deterioration of the disease.
Patients may be advised to refrain from excessive eating in view of the possibility of weight gain.

DRUG INTERACTIONS
The risk of using Risperidone (Risponz) in combination with other medicines has not been systematically evaluated. Risperidone (Risponz) should be used with caution in combination with alcohol and other centrally acting medicines. It may antagonize the effect of levodopa and other dopamine agonists.
Carbamazepine has been shown to decrease the plasma levels of the active antipsychotic fraction of Risperidone (Risponz) . Similar effects may be observed with other hepatic enzyme inducers. On discontinuation of carbamazepine or other hepatic enzyme inducers the dosage of Risperidone (Risponz) should be re-evaluated and, if necessary, decreased.
Phenothiazines, tricyclic antidepressants and some beta-blockers may increase the plasma concentration of Risperidone but not that of the antipsychotic fraction. Fluoxetine may increase the plasma concentration of Risperidone but less so of the anti-psychotic fraction.
When Risperidone (Risponz) is taken together with other highly protein-bound medicines (e.g. diazepam, warfarin, digitoxin, imipramine and propranolol), there is no clinically relevant displacement of either agent from the plasma proteins.

OVERDOSE AND TREATMENT
Reported signs and symptoms have been those resulting from an exaggeration of the medicines known pharmacological effects. Symptoms of acute overdosage include drowsiness, sedation, hypotension tachycardia and extra pyramidal symptoms. In overdose, rare cases of QT-prolongation have been reported.
In the case of acute overdosage, the possibility of multiple medicine involvement should be considered.

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

STORAGE CONDITION
Store at temperatures not exceeding 30°C.
Keep out of reach of children.

AVAILABILITY
Risponz 1: Alu-clear PVC/PVDC Blister pack x 10's (Box of 30's)
Risponz 2 and 3: Alu/PVC/PVDC Blister pack x 10's (Box of 30's)

ADR REPORTING STATEMENT:
For suspected adverse drug reaction, report to the
FDA: www.fda.gov.ph
Seek medical attention immediately at the first sign of any adverse drug reaction.

Reg No.:
Risponz 1: DRP-9961
Risponz 2: DRP-7354
Risponz 3: DRP-7355

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EXP0527

Black
Size : 180 x 300 mm (Front Side)

Black
Size : 180 x 300 mm (Back Side)

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