RESPIROX®

(Risperidone)

ACTION

Risperidone, the active ingredient of Respirox, is a unique selective monoaminergic antagonist that possesses high affinity for the serotonergic 5-HT_2 and the dopaminergic D_2 receptors in the Central Nervous System. It also possesses but to a lower extent some antagonistic effect on alpha$_1$-adrenergic receptors and H_1-histaminergic as well as alpha$_2$-adrenergic receptors. Respirox doesn't have anticholinergic activity. Due to its unique neuroleptic action that is different from the classical neuroleptics, Respirox improves the positive as well as the negative symptoms of schizophrenia with reduced extrapyramidal side effects.

Respirox may also be combined with benzodiazepines in order to obtain additional sedation depending on the individual case.

Respirox is completely absorbed following oral administration. It reaches peak plasma concentrations within 1 to 2 hours. Absorption is not affected by food. Respirox is metabolized by the liver enzymes to 9-hydroxy-risperidone which possesses similar antipsychotic activity as Respirox. The elimination half life is around 3 hours for Respirox and 24 hours for the active metabolite. Steady-state-kinetics is attained after 1 day of treatment for Respirox and after 4 to 5 days for the active metabolite. The plasma protein binding is 88% for Respirox and 77% for the active metabolite. Excretion is mainly through the urine and to a lesser extent through feces.

INDICATIONS

Respirox is an anti-psychotic that is indicated for the treatment of acute and chronic cases of schizophrenia and other psychotic conditions where positive symptoms (e.g. hallucinations, delusions, thought disturbance, hostility and suspiciousness) and/or negative symptoms (e.g. blunted affect, emotional and social withdrawal and poverty of speech) are present. Respirox may also relieve the affective symptoms (such as depression, guilt feelings, anxiety) associated with psychotic cases.

DOSAGE AND ADMINISTRATION

In Adults:

Respirox could be given once or twice daily in doses titrated to 6 mg gradually over three days from the onset of treatment. The usual starting dose of Respirox is 2 mg/day for the first day, then increased to 4 mg in the second day and 6 mg on the third day of treatment, after which the dose requirement of each patient is assessed individually to either keep it unchanged or to increase it up to 8 mg/day. Some patients would require lower doses or a slower titration process according to their individual cases. In most cases, the therapeutic dose would range from 4 to 8 mg/day; high doses (up to 16 mg/day) have been associated with higher risk of side effects occurrence without having significant improvement on efficacy compared to usual therapeutic doses.

Respirox may be administered with or without food.

In Elderly:

Although Respirox is generally well tolerated in the elderly, it is recommended to lower the doses and the subsequent increments to half the usual doses. The recommended starting dose in elderly is 0.5 mg/day given in two divided doses. The dose could then be increased by 0.5 mg b.i.d incremental increases to 1 to 2 mg/day in two divided doses.

In Children:

Respirox in not indicated for children younger than 15 years of age due to lack of clinical experience in this population.

In Renal and Liver Disease:

Respirox could be used but with caution in this group. If decided to give Respirox, the starting dose should be 0.5 mg/day in two divided doses and increased if necessary by 0.5 mg b.i.d increments to 1 to 2 mg/day in two divided doses.

Switching from other antipsychotics:

Gradual discontinuation of the previous treatment while initiating Respirox therapy is recommended.

CONTRAINDICATIONS

Respirox is contra-indicated in patients with known hypersensitivity to the active ingredient (Risperidone) or the added excepients (see excepients section below).

WARNINGS AND PRECAUTIONS

Risperidone should be used with caution in patients with cardiovascular disease such as heart failure, myocardial infarction, conduction abnormalities, dehydration, hypovolaemia or cerebrovascular disease due to increased risk of (orthostatic) hypotension especially in the initial titration phase. If hypotension occurs, a dose reduction is recommended.

Risperidone could be associated with the induction of tardive dyskinesia (involuntary movements of tongue and/or face) but lower than with classical neuroleptics.

Occurrence of extrapyramidal symptoms could add to the development of tardive dyskinesia. If tardive dyskinesia occur, discontinuation of all antipsychotic medications may be appropriate.

Risperidone should be discontinued if symptoms of the Neuroleptic Malignant Syndrome occur during treatment and should not be given to patients with such syndrome. The symptoms of this syndrome are hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated CPK levels and could occur during treatment with classical neuroleptics. Risperidone should be discontinued in this case.

Risperidone may cause worsening of cases of Parkinson's disease, thus Risperidone should only be given with caution.

Risperidone should be given with caution in patients with epilepsy.

Patients should be warned from the possibility of weight gain with Risperidone treatment. In accordance, patients should be advised to avoid excessive eating.

Pregnancy and Lactation:

Risperidone is not recommended for use in pregnant women unless the benefits clearly outweigh the risks.

Risperidone and its metabolite are excreted in human breast milk. Therefore, women receiving Risperidone should not breastfeed.

Ability to drive or operate machinery:

Risperidone may interfere with patients performing tasks requiring mental alertness (such as driving or operating machinery), therefore, it is not advised for patients taking Risperidone to engage in such activities.

Drug interactions

Due to unclear precise mechanism of action, Risperidone should be given with caution in combination with other CNS active medications. Risperidone may antagonize the effect of dopamine agonists (e.g. Levodopa).

Risperidone is metabolized by liver cytochrome CYP IID6 group and thus drug interactions may occur with hepatic enzyme inducers (e.g. Carbamazepine) leading to decreased levels of the active antipsychotic fraction of Risperidone.

Some concomitant medications (e.g. Phenothiazines, tricyclic anti-depressants, Fluoxetine or beta-blockers) may increase the plasma levels of Risperidone. Dose adjustments are appropriate in such cases.

No clinical significant interactions exist between Risperidone and other medications highly bound to plasma proteins.

SIDE EFFECTS

Although Risperidone is generally well tolerated, it is sometimes difficult to differentiate between adverse events and the symptoms of the underlying disease. The most commonly reported side effects include insomnia, agitation, anxiety and headache. Other less common side effects include somnolence, fatigue, dizziness, impaired concentration, constipation, dyspepsia, nausea and vomiting, abdominal pain, blurred vision, priapism, erectile dysfunction, ejaculatory dysfunction, orgastic dysfunction, urinary incontinence, rhinitis, rash and other allergic reactions. Extrapyramidal symptoms (e.g. tremor, rigidity, hypersalivation, bradykinesia, akathisia, acute dystonia) are possible although less frequent than with classical neuroleptics. Such symptoms are usually mild and reversible upon dose reduction and/or administration of antiparkinson medication, if necessary.

Orthostatic hypotension, reflex tachycardia and sometimes hypertension have been observed following administration of Risperidone.

A mild fall in neutrophil and/or thrombocyte count has been reported.

Risperidone may increase the levels of plasma prolactin leading to galactorrhoea, gynecomastia, menstrual cycle disturbances and amenorrhea.

Weight gain has also been reported in patients on Risperidone treatment.

Water intoxication has also been reported in some psychotic patients.

OVERDOSAGE

Overdosage with Risperidone may result in drowsiness, sedation, tachycardia, hypotension and extrapyramidal symptoms. QT-prolongation has been reported in rare cases. No specific antidote for Risperidone exists to date. However, in overdosage cases, supportive measures are indicated, such as maintaining clear airways and adequate oxygenation. Gastric lavage or administration of activated charcoal with a laxative could be considered. Continuous ECG monitoring is advisable to detect possible arrhythmias. If hypotension occurs, administration of fluids or sympathomimetic agents could be considered. Anticholinergic medications could be used if extrapyramidal symptoms occur. Patients could be hospitalized for close monitoring and supervision till symptoms subside.

STORAGE

Store between 15-25°C.

PRESENTATIONS

Tablets:

Respirox 1 mg:	Risperidone 1 mg/tablet
Respirox 2 mg:	Risperidone 2 mg/tablet
Respirox 4 mg:	Risperidone 4 mg/tablet

Excepients: Aerosil 200, Avicel pH102, Lactose Monohydrate (Fast Flow), Corn Starch, Magnesium Stearate and Sodium Lauryl Sulphate. Colouring agents are Opadry II White (1 mg tablets), Aquacota II orange (2 mg tablets), and Opadry II Green (4 mg tablets).

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, 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.

Manufactured by:
HIKMA Pharmaceuticals, Amman-Jordan

Keep medicament out of the reach of children

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