1. NAME OF THE MEDICINAL PRODUCT

RISPERIDONE ORALLY DISINTEGRATING TABLETS USP 1MG

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each Orally Disintegrating Tablet Contains:

Risperidone USP	1 mg
Excipients	Q.S

3. PHARMACEUTICAL FORM

Orally Disintegrating Uncoated Tablet

4. Clinical particulars

4.1 Therapeutic indications

Indicated for the treatment of schizophrenia.

Indicated for the treatment of moderate to severe manic episodes associated with bipolar disorders.

Indicated 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.

Indicated 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 subaverage 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 programme, including psychosocial and educational intervention. It is recommended that risperidone 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.

4.2 Posology and method of administration

Posology

Schizophrenia

Adults

Tablets may be given once daily or twice daily.

Patients should start with 2 mg/day risperidone. The dosage may be increased on the second day to 4 mg. Subsequently, the dosage can be maintained unchanged, or further individualised, 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.

Paediatric population

Risperidone 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

Should be administered on a once daily schedule, starting with 2 mg risperidone. Dosage adjustments, if indicated, should occur at intervals of not less than 24 hours and in dosage increments of 1 mg per day. Risperidone 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 risperidone have not been investigated in patients with manic episodes.
As with all symptomatic treatments, the continued use 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 older people is limited, caution should be exercised.

Paediatric population
Risperidone 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.
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 must be evaluated and justified on an ongoing basis.
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 risperidone.
Irrespective of the indication, starting and consecutive dosing should be halved, and dose titration should be slower for patients with renal or hepatic impairment.
Should be used with caution in these groups of patients.

Method of administration
For oral use. Food does not affect the absorption.
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 (see section 4.8). 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 Risperidone Orodispersible Tablets therapy is initiated is recommended. Also, if medically appropriate, when

switching patients from depot antipsychotics, initiate Risperidone Orodispersible Tablets therapy in place of the next scheduled injection. The need for continuing existing anti-Parkinson medicines should be re-evaluated periodically.

Risperidone Orodispersible Tablets:
Do not open the blister until ready to administer. Remove the tablet from the blister with dry hands. Immediately place the tablet on the tongue. The tablet will begin disintegrating within seconds. Water may be used if desired.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed below:-

- Mannitol
- Croscarmellose sodium
- Magnesium carbonate, heavy
- Ferric Oxide Red (E172)
- Magnesium stearate
- Hydroxypropylcellulose
- Aspartame (E951)
- Saccharin sodium
- Talc
- Flavor peppermint 517
- Levomenthol
- Silica colloidal anhydrous

4.4 Special warnings and precautions for use

No special requirements.

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic-related Interactions

Drugs known to prolong the QT interval

As with other antipsychotics, caution is advised when prescribing risperidone with medicinal products known to prolong the QT interval, such as antiarrhythmics (e.g., quinidine, dysopiramide, procainamide, propafenone, amiodarone, sotalol), tricyclic antidepressant (i.e., amitriptyline), tetracyclic antidepressants (i.e., maprotiline), some antihistamines, other antipsychotics, some antimalarials (i.e., quinine and mefloquine), and with medicines causing electrolyte imbalance (hypokalaemia, hypomagnesiaemia), bradycardia, or those which inhibit the hepatic metabolism of risperidone. This list is indicative and not exhaustive.

Centrally-Acting Drugs and Alcohol

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.

Levodopa and Dopamine Agonists

Risperidone Orodispersible Tablets may antagonise 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.

Drugs with Hypotensive Effect

Clinically significant hypotension has been observed postmarketing with concomitant use of risperidone and antihypertensive treatment.

Paliperidone

Concomitant use of oral Risperidone Orodispersible Tablets 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.

Pharmacokinetic-related Interactions
Food does not affect the absorption of Risperidone Orodispersible Tablets.
Risperidone is mainly metabolized through CYP2D6, and to a lesser extent through CYP3A4. Both risperidone and its active metabolite 9-hydroxy-risperidone are substrates of P-glycoprotein (P-gp). Substances that modify CYP2D6 activity, or substances strongly inhibiting or inducing CYP3A4 and/or P-gp activity, may influence the pharmacokinetics of the risperidone active antipsychotic fraction.

Strong CYP2D6 Inhibitors
Co-administration of Risperidone Orodispersible Tablets with a strong CYP2D6 inhibitor may increase the plasma concentrations of risperidone, but less so of the active antipsychotic fraction. Higher doses of a strong CYP2D6 inhibitor may elevate concentrations of the risperidone active antipsychotic fraction (e.g., paroxetine, see below). It is expected that other CYP 2D6 inhibitors, such as quinidine, may affect the plasma concentrations of risperidone in a similar way. When concomitant paroxetine, quinidine, or another strong CYP2D6 inhibitor, especially at higher doses, is initiated or discontinued, the physician should re-evaluate the dosing of Risperidone Orodispersible Tablets.

CYP3A4 and/or P-gp Inhibitors
Co-administration of Risperidone Orodispersible Tablets with a strong CYP3A4 and/or P-gp inhibitor may substantially elevate plasma concentrations of the risperidone active antipsychotic fraction. When concomitant itraconazole or another strong CYP3A4 and/or P-gp inhibitor is initiated or discontinued, the physician should re-evaluate the dosing of Risperidone Orodispersible Tablets.

CYP3A4 and/or P-gp Inducers
Co-administration of Risperidone Orodispersible Tablets with a strong CYP3A4 and/or P-gp inducer may decrease the plasma concentrations of the risperidone active antipsychotic fraction. When concomitant carbamazepine or another strong CYP3A4 and/or P-gp inducer is initiated or discontinued, the physician should re-evaluate the dosing of Risperidone Orodispersible Tablets. CYP3A4 inducers exert their effect in a time-dependent manner, and may take at least 2 weeks to reach maximal effect after introduction. Conversely, on discontinuation, CYP3A4 induction may take at least 2 weeks to decline.

Highly Protein-bound Drugs
When Risperidone Orodispersible Tablets is taken together with highly protein-bound drugs, there is no clinically relevant displacement of either drug from the plasma proteins.
When using concomitant medication, the corresponding label should be consulted for information on the route of metabolism and the possible need to adjust dosage.

Paediatric population
Interaction studies have only been performed in adults. The relevance of the results from these studies in paediatric patients is unknown.
The combined use of psychostimulants (e.g., methylphenidate) with Risperidone Orodispersible Tablets in children and adolescents did not alter the pharmacokinetics and efficacy of Risperidone Orodispersible Tablets.

Examples
Examples of drugs that may potentially interact or that were shown not to interact with risperidone are listed below:
Effect of other medicinal products on the pharmacokinetics of risperidone

Antibacterials:
Erythromycin, a moderate CYP3A4 inhibitor and P-gp inhibitor, does not change the pharmacokinetics of risperidone and the active antipsychotic fraction.
Rifampicin, a strong CYP3A4 inducer and a P-gp inducer, decreased the plasma concentrations of the active antipsychotic fraction.

Anticholinesterases:
Donepezil and galantamine, both CYP2D6 and CYP3A4 substrated, do not show a clinically relevant effect on the pharmacokinetics of risperidone and the active antipsychotic fraction.

Antiepileptics:
Carbamazepine, a strong CYP3A4 inducer and a P-gp inducer, has been shown to decrease the plasma concentrations of the active antipsychotic fraction of risperidone. Similar effects may be observed with e.g. phenytoin and phenobarbital which also induce CYP 3A4 hepatic enzyme, as well as P-glycoprotein.
Topiramate modestly reduced the bioavailability of risperidone, but not that of the active antipsychotic fraction. Therefore, this interaction is unlikely to be of clinical significance.

Antifungals:
Itraconazole, a strong CYP3A4 inhibitor and a P-gp inhibitor, at a dosage of 200 mg/day increased the plasma concentrations of the active antipsychotic fraction by about 70%, at risperidone doses of 2 to 8 mg/day.
Ketoconazole, a strong CYP3A4 inhibitor and a P-gp inhibitor, at a dosage of 200mg/day increased the plasma concentrations of risperidone and decreased the plasma concentrations of 9-hydroxy-risperidone.

Antipsychotics:
Phenothiazines may increase the plasma concentrations of risperidone but not those of the active antipsychotic fraction.

Antivirals:
Protease inhibitors: No formal study data are available; however, since ritonavir is a strong CYP3A4 inhibitor and a weak CYP2D6 inhibitor, ritonavir and ritonavir-boosted protease inhibitors potentially raise concentrations of the risperidone active antipsychotic fraction.

Beta blockers:
Some beta-blockers may increase the plasma concentrations of risperidone but not those of the active antipsychotic fraction.

Calcium channel blockers:
Verapamil, a moderate inhibitor of CYP3A4 and an inhibitor of P-gp, increases the plasma concentration of risperidone and the active antipsychotic fraction.

Gastrointestinal drugs:
H2-receptor antagonists: Cimetidine and ranitidine, both weak inhibitors of CYP2D6 and CYP3A4, increased the bioavailability of risperidone, but only marginally that of the active antipsychotic fraction.

SSRIs and Tricyclic antidepressants:
Fluoxetine, a strong CYP2D6 inhibitor, increases the plasma concentration of risperidone, but less so of the active antipsychotic fraction.
Paroxetine, a strong CYP2D6 inhibitor, increases the plasma concentrations of risperidone, but, at dosages up to 20 mg/day, less so of the active antipsychotic fraction. However, higher doses of paroxetine may elevate concentrations of the risperidone active antipsychotic fraction.
Tricyclic antidepressants 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.
Sertraline, a weak inhibitor of CYP2D6, and fluvoxamine, a weak inhibitor of CYP3A4, at dosages up to 100 mg/day are not associated with clinically significant changes in concentrations of the risperidone active antipsychotic fraction. However, doses higher than 100 mg/day of sertraline or fluvoxamine may elevate concentrations of the risperidone active antipsychotic fraction.

Effect of risperidone on the pharmacokinetics of other medicinal products

Antiepileptics:
Risperidone does not show a clinically relevant effect on the pharmacokinetics of valproate or topiramate.

Antipsychotics:
Aripiprazole, a CYP2D6 and CYP3A4 substrate: Risperidone tablets or injections did not affect the pharmacokinetics of the sum of aripiprazole and its active metabolite, dehydroaripiprazole.

Digitalis glycosides:
Risperidone does not show a clinically relevant effect on the pharmacokinetics of digoxin.

Lithium:
Risperidone does not show a clinically relevant effect on the pharmacokinetics of lithium.

4.6 Pregnancy and Lactation

Pregnancy
There are no adequate data from the use of risperidone in pregnant women. Risperidone was not teratogenic in animal studies but other types of reproductive toxicity were seen. The potential risk for humans is unknown.
Neonates exposed to antipsychotics (including Risperidone Orodispersible Tablets) 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.

Risperidone Orodispersible Tablets should not be used during pregnancy unless clearly necessary. If discontinuation during pregnancy is necessary, it should not be done abruptly.

Breast-feeding
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.

Fertility
As with other drugs that antagonize dopamine D2 receptors, Risperidone Orodispersible Tablets elevates prolactin level. Hyperprolactinemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotropin secretion. This, in turn, may inhibit reproductive function by impairing gonadal steroidogenesis in both female and male patients.
There were no relevant effects observed in the non-clinical studies.

4.7 Effects on ability to drive and use machines

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.

4.8 Undesirable effects

The most frequently reported adverse drug reactions (ADRs) (incidence ≥10%) are: Parkinsonism, sedation/somnolence, headache, and insomnia.

The ADRs that appeared to be dose-related included parkinsonism and akathisia.

The following are all the ADRs that were reported in clinical trials and postmarketing experience with risperidone by frequency category estimated from Risperidone Orodispersible Tablets clinical trials. The following terms and frequencies are applied: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000) and very rare (<1/10,000)

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Adverse Drug Reactions by System Organ Class and Frequency

Infections and infestations	
Common	Pneumonia, Influenza, Bronchitis, Upper respiratory tract infection, Urinary tract infection, Sinusitis, Ear infection
Uncommon	Viral infection, Tonsillitis, Cellulitis localized infection, Acarodermatitis, Respiratory tract infection, Cystitis, Onychomycosis, Eye infection
Rare	Infection
Blood and lymphatic system disorders	
Uncommon	Neutropenia, White blood cell count decreased, Anaemia, Thrombocytopenia, Haematrocrit decreased, Eosinophil count increased
Rare	Agranulocytosis[C]
Immune system disorders	
Uncommon	Hypersensitivity
Rare	Anaphylactic reaction[C]
Endocrine disorders	
Common	Hyperprolactinaemia[a]
Rare	Inappropriate antidiuretic hormone secretion, glucose urine present
Metabolism and nutrition disorders	
Common	Increased appetite, Decreased appetite, Weight increased
Uncommon	Diabetes mellitus [b], Hyperglycaemia, Polydipsia, Weight decreased, Anorexia, Blood cholesterol increased
Rare	Water intoxication[c], Hypoglycaemia, Hyperinsulinaemia[c], Blood triglycerides increased
Very rare	Diabetic ketoacidosis
Psychiatric disorders	
Very common	Insomnia[d]
Common	Anxiety, Agitation, Sleep disorder, Depression
Uncommon	Confusional state, Mania, Libido decreased, Nervousness, Nightmare
Rare	Anorgasmia, Blunted affect
Nervous system disorders	
Very common	Sedation/ Somnolence, Parkinsonism[d], Headache
Common	Akathisia[d], Dizziness, Tremor, Dystonia[d], Dyskinesia[d]
Uncommon	Tardive dyskinesia, Cerebral ischaemia, Unresponsive to stimuli, loss of consciousness, Depressed level of consciousness, Convulsion[d], Syncope, Psychomotor hyperactivity, Balance disorder, Coordination abnormal, Dizziness postural, Disturbance in attention, Dysarthria, Dysgeusia, Hypoaesthesia, paraesthesia
Rare	Neuroleptic malignant syndrome, Diabetic coma, Cerebrovascular disorder, Head titubation
Eye disorders	
Common	Vision blurred, Conjunctivitis
Uncommon	Ocular hyperaemia, Dry eye, Lacrimation increased, Photophobia
Rare	Glaucoma, Eye movement disorder, Eye rolling, Eyelid margin crusting, Floppy iris syndrome (intraoperative)[C]
Ear and labyrinth disorders	
Uncommon	Ear pain, Tinnitus, Vertigo
Cardiac disorders	
Common	Tachycardia
Uncommon	Atrial fibrillation, Atrioventricular block, Conduction disorder, Electrocardiogram QT

	prolonged, Bradycardia, Electrocardiogram abnormal, Palpitations
Rare	Sinus arrhythmia
Vascular disorders	
Common	Hypertension
Uncommon	Hypotension, Orthostatic hypotension, Flushing
Rare	Pulmonary embolism, Venous thrombosis
Respiratory, thoracic and mediastinal disorders	
Common	Dyspnoea, Epistaxis, Cough, Nasal congestion, Pharyngolaryngeal pain
Uncommon	Wheezing, Pneumonia aspiration, Pulmonary congestion, Respiratory disorder, Rales, Respiratory tract congestion, Dysphonia
Rare	Sleep apnoea syndrome, Hyperventilation
Gastrointestinal disorders	
Common	Vomiting, Diarrhoea, Constipation, Nausea, Abdominal pain, Abdominal discomfort, Dyspepsia, Dry mouth, Toothache
Uncommon	Dysphagia, Gastroenteritis, Faecal incontinence, Faecaloma, Flatulence
Rare	Intestinal obstruction, Pancreatitis, Swollen tongue, Cheilitis
Very rare	Ileus
Skin and subcutaneous tissue disorders	
Common	Rash, Erythema
Uncommon	Skin lesion, Skin disorder, Pruritus, Acne, Skin discoloration, Alopecia, Seborrhoeic dermatitis, Dry skin, Hyperkeratosis, Eczema, Urticaria
Rare	Drug eruption, Dandruff
Very rare	Angioedema
Musculoskeletal and connective tissue disorders	
Common	Arthralgia, Back pain, Muscle spasms, Musculoskeletal pain
Uncommon	Blood creatine phosphokinase increased, Posture abnormal, Joint stiffness, Joint swelling muscular weakness, Neck pain
Rare	Rhabdomyolysis
Renal and urinary disorders	
Common	Urinary incontinence
Uncommon	Dysuria, Urinary retention, Pollakiuria
Pregnancy, puerperium and neonatal conditions	
Rare	Drug withdrawal syndrome neonatal[c]
Reproductive system and breast disorders	
Uncommon	Amenorrhoea, Sexual dysfunction, Erectile dysfunction, Ejaculation disorder, Galactorrhoea, Gynaecomastia, Menstrual disorder[d], Vaginal discharge, Breast pain, Breast discomfort
Rare	Priapism[c], Menstruation delayed, Breast engorgement, Breast enlargement, Breast discharge
General disorders and administration site conditions	
Common	Pyrexia, Fatigue, Oedema[d], Asthenia, Chest pain, Pain
Uncommon	Face oedema, Gait abnormal, Feeling abnormal, Thirst, Chest discomfort, Chills, Body temperature increased, Discomfort
Rare	Hypothermia, Body temperature decreased, Drug withdrawal syndrome, Peripheral coldness, Induration[c]
Hepatobiliary disorders	

Uncommon	Transaminases increased, Gamma-glutamyl transferase increased, Hepatic enzyme increased
Rare	Jaundice
Injury, poisoning and procedural complications	
Common	Fall
Uncommon	Procedural pain

[a] Hyperprolactinemia can in some cases lead to gynaecomastia, menstrual disturbances, amenorrhoea, anovulation, galactorrhea, fertility disorder, decreased libido, erectile dysfunction.

[b] In placebo-controlled trials diabetes mellitus was reported in 0.18% in risperidone-treated subjects compared to a rate of 0.11% in placebo group. Overall incidence from all clinical trials was 0.43% in all risperidone-treated subjects.

[c] Not observed in Risperidone Orodispersible Tablets clinical studies but observed in post-marketing environment with risperidone.

[d] Extrapyramidal disorder may occur: Parkinsonism (salivary hypersecretion, musculoskeletal stiffness, parkinsonism, drooling, cogwheel rigidity, bradykinesia, hypokinesia, masked facies, muscle tightness, akinesia, nuchal rigidity, muscle rigidity, parkinsonian gait, and glabellar reflex abnormal, parkinsonian rest tremor), akathisia (akathisia, restlessness, hyperkinesia, and restless leg syndrome), tremor, dyskinesia (dyskinesia, muscle twitching, choreoathetosis, athetosis, and myoclonus), dystonia.

Dystonia includes dystonia, hypertonia, torticollis, muscle contractions involuntary, muscle contracture, blepharospasm, oculogyration, tongue paralysis, facial spasm, laryngospasm, myotonia, opisthotonus, oropharyngeal spasm, pleurothotonus, tongue spasm, and trismus. It should be noted that a broader spectrum of symptoms are included, that do not necessarily have an extrapyramidal origin. **Insomnia** includes: initial insomnia, middle insomnia; **Convulsion** includes: Grand mal convulsion; **Menstrual disorder** includes: Menstruation irregular, oligomenorrhoea; **Oedema** includes: generalised oedema, oedema peripheral, pitting oedema.

Undesirable effects noted with paliperidone formulations

Paliperidone is the active metabolite of risperidone, therefore, the adverse reaction profiles of these compounds (including both the oral and injectable formulations) are relevant to one another. In addition to the above adverse reactions, the following adverse reaction has been noted with the use of paliperidone products and can be expected to occur with Risperidone Orodispersible Tablets.

Cardiac disorders: Postural orthostatic tachycardia syndrome

Class effects

As with other antipsychotics, very rare cases of QT prolongation have been reported postmarketing with risperidone. Other class-related cardiac effects reported with antipsychotics which prolong QT interval include ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia, sudden death, cardiac arrest and Torsades de Pointes.

Venous thromboembolism

Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis, have been reported with antipsychotic drugs (frequency unknown).

Weight gain

The proportions of Risperidone Orodispersible Tablets and placebo-treated adult patients with schizophrenia meeting a weight gain criterion of ≥ 7% of body weight were compared in a pool of 6- to 8-week, placebo-controlled trials, revealing a statistically significantly greater incidence of weight gain for Risperidone Orodispersible Tablets (18%) compared to placebo (9%). In a pool of placebo-controlled 3-week studies in adult patients with acute mania, the incidence of weight increase of ≥ 7% at endpoint was comparable in the Risperidone Orodispersible Tablets (2.5%) and placebo (2.4%) groups, and was slightly higher in the active-control group (3.5%).

In a population of children and adolescents with conduct and other disruptive behaviour disorders, in long- term studies, weight increased by a mean of 7.3 kg after 12 months of treatment. The expected weight gain for normal children between 5-12 years of age is 3 to 5 kg per year. From 12-16 years of age, this magnitude of gaining 3 to 5 kg per year is maintained for girls, while boys gain approximately 5 kg per year.

Additional information on special populations

Adverse drug reactions that were reported with higher incidence in elderly patients with dementia or paediatric patients than in adult populations are described below:

Elderly patients with dementia

Transient ischaemic attack and cerebrovascular accident were ADRs reported in clinical trials with a frequency of 1.4% and 1.5%, respectively, in older people with dementia. In addition, the following ADRs were reported with a frequency ≥5% in older people with dementia and with at least twice the frequency seen in other adult populations: urinary tract infection, peripheral oedema, lethargy, and cough.

Paediatric population

In general, type of adverse reactions in children is expected to be similar to those observed in adults.

The following ADRs were reported with a frequency ≥5% in paediatric patients (5 to 17 years) and with at least twice the frequency seen in clinical trials in adults: somnolence/sedation, fatigue, headache, increased appetite, vomiting, upper respiratory tract infection, nasal congestion, abdominal pain, dizziness, cough, pyrexia, tremor, diarrhoea, and enuresis.

The effect of long-term risperidone treatment on sexual maturation and height has not been adequately studied (see 4.4, subsection "Paediatric Population").

4.9 Overdose

Symptoms
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.

Treatment
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 a 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 Orodispersible Tablets. 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, an anticholinergic medicincal product should be administered. Close medical supervision and monitoring should continue until the patient recovers.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Other antipsychotics, ATC code: N05AX08

Mechanism of action

Risperidone is a selective monoaminergic antagonist with unique properties. It has a high affinity for serotoninergic 5-HT_2 and dopaminergic D_2 receptors. Risperidone binds also to alpha$_1$-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 effect liability and extend the therapeutic activity to the negative and affective symptoms of schizophrenia.

Pharmacodynamic effects

Clincal efficacy

Schizophrenia

The efficacy of risperidone in the short-term treatment of schizophrenia was established in four studies, 4- to 8-weeks in duration, which enrolled over 2500 patients who met DSM-IV criteria for schizophrenia. In a 6- week, placebo-controlled trial involving titration of risperidone in doses up to 10 mg/day administered twice daily, risperidone was superior to placebo on the Brief Psychiatric Rating Scale (BPRS) total score. In an 8- week, placebo-controlled trial involving four fixed doses of risperidone (2, 6, 10, and 16 mg/day, administered twice daily), all four risperidone groups were superior to placebo on the Positive and Negative Syndrome Scale (PANSS) total score. In an 8-week, dose comparison trial involving five fixed doses of risperidone (1, 4, 8, 12, and 16 mg/day administered twice-daily), the 4, 8, and 16 mg/day risperidone dose groups were superior to the 1 mg risperidone dose group on PANSS total score. In a 4-week, placebo- controlled dose comparison trial involving two fixed doses of risperidone (4 and 8 mg/day administered once daily), both risperidone dose groups were superior to placebo on several PANSS measures, including total PANSS and a response measure (>20% reduction in PANSS total score). In a longer-term trial, adult outpatients predominantly meeting DSM-IV criteria for schizophrenia and who had been clinically stable for at least 4 weeks on an antipsychotic medicinal product were randomised to risperidone 2 to 8 mg/day or to haloperidol for 1 to 2 years of observation for relapse. Patients receiving risperidone experienced a significantly longer time to relapse over this time period compared to those receiving haloperidol.

Manic episodes in bipolar disorder

The efficacy of risperidone monotherapy in the acute treatment of manic episodes associated with bipolar I disorder was demonstrated in three double-blind, placebo-controlled monotherapy studies in approximately 820 patients who had bipolar I disorder, based on DSM-IV criteria. In the three studies, risperidone 1 to 6 mg/day (starting dose 3 mg in two studies and 2 mg in one study) was shown to be significantly superior to placebo on the pre-specified primary endpoint, i.e., the change from baseline in total Young Mania Rating Scale (YMRS) score at Week 3. Secondary efficacy outcomes were generally consistent with the primary outcome. The percentage of patients with a decrease of ≥ 50% in total YMRS score from baseline to the 3-week endpoint was significantly higher for risperidone than for placebo. One of the three studies included a haloperidol arm and a 9-week double-blind maintenance phase. Efficacy was maintained throughout the 9-week maintenance treatment period. Change from baseline in total YMRS showed continued improvement and was comparable between risperidone and haloperidol at Week 12.

The efficacy of risperidone in addition to mood stabilisers in the treatment of acute mania was demonstrated in one of two 3-week double-blind studies in approximately 300 patients who met the DSM-IV criteria for bipolar I disorder. In one 3-week study, risperidone 1 to 6 mg/day starting at 2 mg/day in addition to lithium or valproate was superior to lithium or valproate alone on the pre-specified primary endpoint, i.e., the change from baseline in YMRS total score at Week 3. In a second 3-week study, risperidone 1 to 6 mg/day starting at 2 mg/day, combined with lithium, valproate, or carbamazepine was not superior to lithium, valproate, or carbamazepine alone in the reduction of YMRS total score. A possible explanation for the failure of this study was induction of risperidone and 9-hydroxy-risperidone clearance by carbamazepine, leading to subtherapeutic levels of risperidone and 9-hydroxy-risperidone. When the carbamazepine group was excluded in a post-hoc analysis, risperidone combined with lithium or valproate was superior to lithium or valproate alone in the reduction of YMRS total score.

Persistent aggression in dementia

The efficacy of risperidone in the treatment of Behavioural and Psychological Symptoms of Dementia (BPSD), which includes behavioural disturbances, such as aggressiveness, agitation, psychosis, activity, and affective disturbances was demonstrated in three double-blind, placebo-controlled studies in 1150 older people with moderate to severe dementia. One study included fixed risperidone doses of 0.5, 1, and 2 mg/day. Two flexible-dose studies included risperidone dose groups in the range of 0.5 to 4 mg/day and 0.5 to 2 mg/day, respectively. Risperidone showed statistically significant and clinically important effectiveness in treating aggression and less consistently in treating agitation and psychosis in older people with dementia (as measured by the Behavioural Pathology in Alzheimer's Disease Rating Scale [BEHAVE-AD] and the Cohen-Mansfield Agitation Inventory [CMAI]). The treatment effect of risperidone was independent of Mini-Mental State Examination (MMSE) score (and consequently of the severity of dementia); of sedative properties of risperidone; of the presence or absence of psychosis; and of the type of dementia, Alzheimer's, vascular, or mixed.

Paediatric population

Conduct disorder
The efficacy of risperidone in the short-term treatment of disruptive behaviours was demonstrated in two double-blind placebo-controlled studies in approximately 240 patients 5 to 12 years of age with a DSM-IV diagnosis of disruptive behaviour disorders (DBD) and borderline intellectual functioning or mild or moderate mental retardation/learning disorder. In the two studies, risperidone 0.02 to 0.06 mg/kg/day was significantly superior to placebo on the pre-specified primary endpoint, i.e., the change from baseline in the Conduct Problem subscale of the Nisonger-Child Behaviour Rating Form (N-CBRF) at Week 6.

5.2 Pharmacokinetic properties

Risperidone is metabolised to 9-hydroxy-risperidone, which has a similar pharmacological activity to risperidone (see *Biotransformation and Elimination*).

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 alpha1-acid glycoprotein. The plasma protein binding of risperidone is 90% that of 9-hydroxy- risperidone is 77%.

Biotransformation and elimination
Risperidone is metabolised 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 metabolisers convert risperidone rapidly into 9-hydroxy-risperidone, whereas poor CYP 2D6 metabolisers convert it much more slowly. Although extensive metabolisers have lower risperidone and higher 9-hydroxy-risperidone concentrations than poor metabolisers, 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 metabolisers 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 metabolised by cytochrome P450 isozymes, including CYP 1A2, CYP 2A6, CYP 2C8/9/10, CYP 2D6, CYP 2E1, CYP 3A4, and CYP 3A5. One week after administration, 70% of the dose is excreted in the urine and 14% in the faeces. 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.

Linearity/non-linerarity
Risperidone plasma concentrations are dose-proportional within the therapeutic dose-range.

Elderly, hepatic and renal impairment
A single-dose PK-study with oral risperidone showed on average a 43% higher active antipsychotic fraction plasma concentrations, a 38% longer half-life and a reduced clearance of the active antipsychotic fraction by 30% in the elderly.
In adults with moderate renal disease the clearance of the active moiety was ~48% of the clearance in young healthy adults. In adults with severe renal disease the clearance of the active moiety was ~31% of the clearance in young healthy adults. The half-life of the active moiety was 16.7 h in young adults, 24.9 h in adults with moderate renal disease (or ~1.5 times as long as in young adults), and 28.8 h in those with severe renal disease (or ~1.7 times as long as in young adults). Risperidone plasma concentrations were normal in patients with liver insufficiency, but the mean free fraction of risperidone in plasma was increased by 37.1%.
The oral clearance and the elimination half-life of risperidone and of the active moiety in adults with moderate and severe liver impairment were not significantly different from those parameters in young healthy adults.

Paediatric population
The pharmacokinetics of risperidone, 9-hydroxy-risperidone and the active antipsychotic fraction in children are similar to those in adults.

Gender, race and smoking habits
A population pharmacokinetic analysis revealed no apparent effect of gender, race or smoking habits on the pharmacokinetics of risperidone or the active antipsychotic fraction.

5.3 Preclinical safety data

In (sub) chronic toxicity studies, in which dosing was started in sexually immature rats and dogs, dose- dependent effects were present in male and female genital tract and mammary gland. These effects were related to the increased serum prolactin levels, resulting from the dopamine D_2-receptor blocking activity of risperidone. In addition, tissue culture studies suggest that cell growth in human breast tumours may be stimulated by prolactin. Risperidone was not teratogenic in rat and rabbit. In rat reproduction studies with risperidone, adverse effects were seen on mating behaviour of the parents, and on the birth weight and survival of the offspring. In rats, intrauterine exposure to risperidone was associated with cognitive deficits in adulthood. Other dopamine antagonists, when administered to pregnant animals, have caused negative effects on learning and motor development in the offspring. In a toxicity study in juvenile rats, increased pup mortality and a delay in physical development was observed. In a 40-week study with juvenile dogs, sexual maturation was delayed. Based on AUC, long bone growth was not affected in dogs at 3.6-times the maximum human exposure in adolescents (1.5 mg/day); while effects on long bones and sexual maturation were observed at 15 times the maximum human exposure in adolescents.

Risperidone was not genotoxic in a battery of tests. In oral carcinogenicity studies of risperidone in rats and mice, increases in pituitary gland adenomas (mouse), endocrine pancreas adenomas (rat), and mammary gland adenomas (both species) were seen. These tumours can be related to prolonged dopamine D_2 antagonism and hyperprolactinaemia. The relevance of these tumour findings in rodents in terms of human risk is unknown. In vitro and in vivo, animal models show that at high doses risperidone may cause QT interval prolongation, which has been associated with a theoretically increased risk of torsade de pointes in patients.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Betadex BP
Mannitol BP
Microcrystalline Cellulose BP
Essential liquid of pipermint flavor IH
Cross povidone BP
Crosscarmelose sodium BP
Neotame swetener USP-NF
Magnesium stearate BP

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Nature and contents of container<and special equipment for use, administration or implantation>

Packing: 3 X 10 Tablets in Alu-Alu Blister Pack

Primary Packing: Alu/Alu Blister of 10 Tablets is packed in printed aluminium foil on one side and plain aluminium foil on other side.

Secondary Packing: Such 3 Blisters are packed in printed carton along with package insert.

6.5 Special precautions for disposal <and other handling>

No special requirements.

7 <APPLICANT/MANUFACTURER>

ENDURANCE HEALTHCARE LTD.
Address: C-1B 305/2, 3, 4& 5, G.I.D.C,
KERALA (BAVLA),
Dist: AHMEDABAD, GUJARAT, INDIA.
Phone: (02714) 268315, 268386
Fax: (02714) 268769
Email: info@endurancehealthcare.com

ENDURANCE HEALTHCARE PRIVATE LIMITED AHMEDABAD

FOIL	Size:210 mm Alu-Alu Bl Printed Foil
Packing : 10 Tablets in One Strip	GSM:0.25 micron
Specification: 0.25 micron Alu-Alu BL Foil DSO	Colour: Black
	Art work No.: Material Code:

Andro 1mg
DÉSINTÉGRATION ORALE
Rispéridone à désintégration orale
Comprimés USP 1mg

Andro 1mg
ORALLY DISINTEGRATING
Risperidone orally disintegrating
Tablets USP 1mg

Andro 1mg
DÉSINTÉGRATION ORALE
Rispéridone à désintégration orale
Comprimés USP 1mg

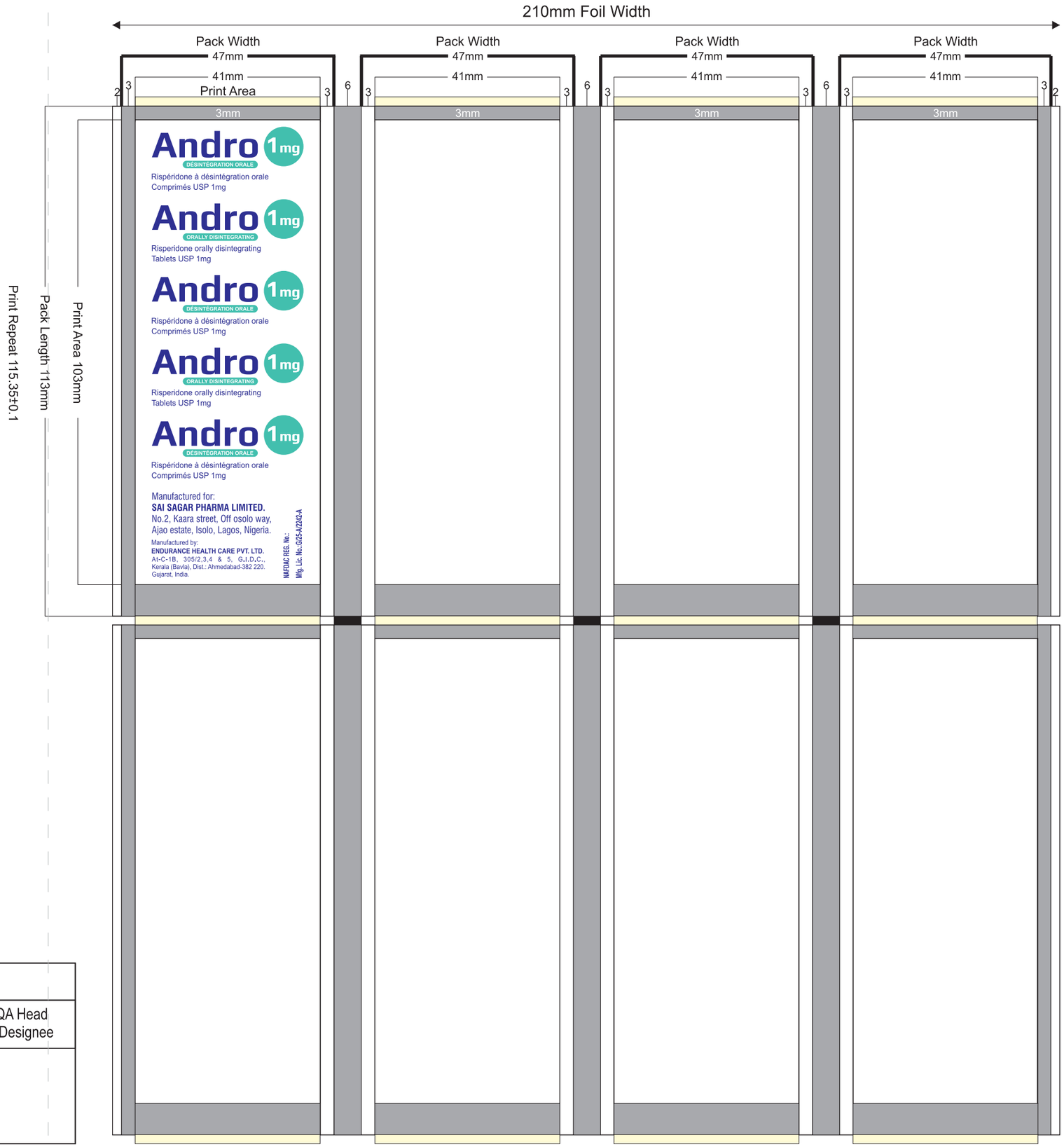
Andro 1mg
ORALLY DISINTEGRATING
Risperidone orally disintegrating
Tablets USP 1mg

Andro 1mg
DÉSINTÉGRATION ORALE
Rispéridone à désintégration orale
Comprimés USP 1mg

Manufactured for:
SAI SAGAR PHARMA LIMITED.
No.2, Kaara street, Off osolo way,
Ajao estate, Isolo, Lagos, Nigeria.
Manufactured by:
ENDURANCE HEALTH CARE PVT. LTD.
At-C-1B, 305/2,3,4 & 5, G.I.D.C.,
Kerala (Bavla), Dist.: Ahmedabad-382 220.
Gujarat, India.

NAFDAC REG. No.:
Mfg. Lic. No.:G/25-A/2242-A

Sign For Artwork Approval				Date	
	Design Officer/Designee	F&D Officer/Designee	QC Head Designee	Production Head/Designee	QA Head /Designee
Stallion LABORATORIES PVT. LTD.					



BOX	Size:L-117 x W-22 x H-51mm
Packing :3 x 10 Tablets Alu-Alu Blister	GSM:300 gsm
Specification: FBB Board 32 gsm, UV Drip off, Window Varnish, Brand Name Emboss, Brail	Colour:CMYK
	Art work No.: Material Code:

Sign For Artwork Approval				Date	
	Design Officer/Designee	F&D Officer/Designee	QC Head Designee	Production Head/Designee	QA Head /Designee
Stallion LABORATORIES PVT. LTD.					

front english 145x255mm french back

Andro

Risperidone orally disintegrating
Tablets USP 1 / 2 mg

Dosage Form: Orally Disintegrating Tablets

Product Description: White to off white colored, round shape uncoated biconvex orally disintegrating tablet having both sides plain.

Composition:
Each orally disintegrating tablet contains:
Risperidone USP.....1/2mg
Excipients.....Q.S.

Mechanism of Action :
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.

Indications:
Risperidone Tabletsis indicated for the treatment of schizophrenia.
Risperidone Tablets is indicated for the treatment of moderate to severe manic episodes associated with bipolar disorders.
Risperidone Tabletsis indicated 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.
Risperidone Tabletsis indicated 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 subaverage intellectual functioning or mental retardation diagnosed according to DSM-IV criteria, in whom the severity of aggressive or other disruptive behaviours require pharmacologic treatment. Pharmacological treatment should be an integral part of a more comprehensive treatment programme, including psychosocial and educational intervention. It is recommended that risperidone 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 the active substance or to any of the excipients.
Dosage and Administration:
Route of Administration: Oral

Schizophrenia
Adults
Risperidone Tablets may be given once daily or twice daily.
Patients should start with 2 mg/day risperidone. The dosage may be increased on the second day to 4 mg. Subsequently, the dosage can be maintained unchanged, or further individualised, 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.
Paediatric population
Risperidone is not recommended for use in children below age 18 with schizophrenia due to a lack of data on efficacy.

Adverse reactions:
The most frequently reported adverse reactions associated with the use of olanzapine were somnolence, weight gain, eosinophilia, elevated prolactin, cholesterol, glucose and triglyceride levels, glucosuria, increased appetite, dizziness, akathisia, parkinsonism, dyskinesia, orthostatic hypotension, anticholinergic effects, transient asymptomatic elevations of hepatic transaminases, rash, asthenia, fatigue and oedema.

Drug Interactions:
Drugs known to prolong the QT interval
As with other antipsychotics, caution is advised when prescribing risperidone with medicinal products known to prolong the QT interval, such as antiarrhythmics (e.g., quinidine, dysopiramide, procainamide, propafenone, amiodarone, sotalol), tricyclic antidepressants (i.e., amitriptyline), tetracyclic antidepressants (i.e., maprotiline), some antihistamines, other antipsychotics, some antimalarials (i.e., quinine and mefloquine), and with medicines causing electrolyte imbalance (hypokalaemia, hypomagnesiaemia), bradycardia, or those which inhibit the hepatic metabolism of risperidone. This list is indicative and not exhaustive.
Centrally-Acting Drugs and Alcohol
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.
Levodopa and Dopamine Agonists
Risperidone Tabletsmay antagonise 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.
Drugs with Hypotensive Effect
Clinically significant hypotension has been observed postmarketing with concomitant use of risperidone and antihypertensive treatment.
Paliperidone
Concomitant use of oral Risperidone Tablets 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.

Pregnancy and Lactation:
Pregnancy
There are no adequate data from the use of risperidone in pregnant women. Risperidone was not teratogenic in animal studies but other types of reproductive toxicity were seen. The potential risk for humans is unknown.
Neonates exposed to antipsychotics (including Risperidone Tablets) 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.
Risperidone Tablets should not be used during pregnancy unless clearly necessary. If discontinuation during pregnancy is necessary, it should not be done abruptly.
Breast-feeding
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.

Precaution /Warnings:
- Elderly patients with dementia
- Increased mortality in elderly people with dementia
- In a meta-analysis of 17 controlled trials of atypical antipsychotics, including Risperidone Tablets, elderly patients with dementia treated with atypical antipsychotics have an increased mortality compared to placebo. In placebo-controlled trials with oral Risperidone Tablets in this population, the incidence of mortality was 4.0% for Risperidone Tablets - treated patients compared to 3.1% for placebo-treated patients. The odds ratio (95% exact confidence interval) was 1.21 (0.7, 2.1). The mean age (range) of patients who died was 86 years (range 67-100). Data from two large observational studies showed that elderly people with dementia who are treated with conventional antipsychotics are also at a small increased risk of death compared with those who are not treated. There are insufficient data to give a firm estimate of the precise magnitude of the risk and the cause of the increased risk is not known. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear.
- Concomitant use with furosemide
- In the Risperidone Tabletsplacebo-controlled trials in elderly patients with dementia, a higher incidence of mortality was observed in patients treated with furosemide plus risperidone (7.3%; mean age 89 years, range 75-97) when compared to patients treated with risperidone alone (3.1%; mean age 84 years, range 70-96) or furosemide alone (4.1%; mean age 80 years, range 67-90). The increase in mortality in patients treated with furosemide plus risperidone was observed in two of the 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 treatment 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 have been seen in randomised placebo controlled clinical trials in the dementia population with some atypical antipsychotics. The pooled data from six placebo-controlled studies with Risperidone Tablets in mainly elderly patients (>65 years of age) with dementia showed that CVAEs (serious and non-serious, combined) occurred in 3.3% (33/1009) of patients treated with risperidone and 1.2% (8/712) of patients treated with placebo. The odds ratio (95% exact confidence interval) was 2.96 (1.34, 7.50). The mechanism for this increased risk is not known. An increased risk cannot be excluded for other antipsychotics or other patient populations. Risperidone Tablets 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 Tabletsin 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 Tabletsshould 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.

Overdose and Treatments:
Symptoms
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 Tabletsand paroxetine.
In case of acute overdose, the possibility of multiple drug involvement should be considered.
Treatment
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 Tablets. 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, an anticholinergic medicinal product should be administered. Close medical supervision and monitoring should continue until the patient recovers.

Packing: 3 x 10 Tablets Alu-Alu Blister Pack

Shelf-life: 36 Months

Storage Condition: Store in a cool & dry place protected from light

Manufactured by:
ENDURANCE HEALTH CARE PVT. LTD.
At-C-1B, 305/2,3,4 & 5, G.I.D.C., Kerala (Bavla),
Dist.: Ahmedabad-382 220. Gujarat, India.

Marketed by: **SAI SAGAR PHARMA LIMITED.**
No.2, Kaara street, Off osolo way, Ajao estate,
Isolo, Lagos, Nigeria.

Andro

Rispéridone à désintégration orale
Comprimés USP 1 / 2 mg

Forme posologique : Comprimés à désintégration orale

Description du produit : Comprimé blanc à blanc cassé, de forme ronde, non enrobé, biconvexe, à désintégration orale, dont les deux faces sont lisses.

Composition:
Chaque comprimé à désintégration orale contient :
Rispéridone USP.....1/2mg
Excipients.....Q.S.

Mécanisme d'action :
La rispéridone est un antagoniste monoaminergique sélectif aux propriétés uniques. Il a une grande affinité pour les récepteurs sérotoninergiques 5-HT2 et dopaminergiques D2. La rispéridone se lie également aux récepteurs alpha1-adrénergiques et, avec une plus faible affinité, aux récepteurs H1-histaminergiques et alpha2-adrénergiques. La rispéridone n'a pas d'affinité pour les récepteurs cholinergiques. Bien que la rispéridone soit un puissant antagoniste D2, qui est considéré comme améliorant les symptômes positifs de la schizophrénie, elle provoque moins de dépression de l'activité motrice et d'induction de catalepsie que les antipsychotiques classiques. Un antagonisme central équilibré de la sérotonine et de la dopamine peut réduire la responsabilité des effets secondaires extrapyramidaux et étendre l'activité thérapeutique aux symptômes négatifs et affectifs de la schizophrénie.

Les indications:
Risperidone Tabletsis est indiqué pour le traitement de la schizophrénie.
Les comprimés de rispéridone sont indiqués pour le traitement des épisodes maniaques modérés à sévères associés aux troubles bipolaires.
Risperidone Tablet est indiqué pour le traitement à court terme (jusqu'à 6 semaines) de l'agressivité persistante chez les patients atteints de démence d'Alzheimer modérée à sévère ne répondant pas aux approches non pharmacologiques et lorsqu'il existe un risque d'atteinte à soi-même ou à autrui.
Rispéridone Comprimé est indiqué dans le traitement symptomatique de courte durée (jusqu'à 6 semaines) de l'agressivité persistante dans les troubles des conduites chez l'enfant à partir de 5 ans et l'adolescent présentant un fonctionnement intellectuel inférieur à la moyenne ou un retard mental diagnostiqué selon les critères du DSM-IV, chez qui le la gravité des comportements agressifs ou autres comportements perturbateurs nécessitent un traitement pharmacologique. Le traitement pharmacologique devrait faire partie intégrante d'un programme de traitement plus complet, comprenant une intervention psychosociale et éducative. Il est recommandé que la rispéridone soit prescrite par un spécialiste en neurologie de l'enfant et en psychiatrie de l'enfant et de l'adolescent ou par des médecins connaissant bien le traitement des troubles des conduites de l'enfant et de l'adolescent.

Contre-indications :
Hypersensibilité à la substance active ou à l'un des excipients.
Dosage et administration:
Voie d'administration : Orale

Schizophrénie
Adultes
Les comprimés de rispéridone peuvent être administrés une fois par jour ou deux fois par jour.
Les patients doivent commencer par 2 mg/jour de rispéridone. La posologie peut être augmentée le deuxième jour à 4 mg. Par la suite, la posologie peut être maintenue inchangée ou encore individualisée, si nécessaire. La plupart des patients bénéficieront de doses quotidiennes comprises entre 4 et 6 mg. Chez certains patients, une phase de titration plus lente et une dose initiale et d'entretien plus faible peuvent être appropriées.
Les doses supérieures à 10 mg/jour n'ont pas démontré une efficacité supérieure aux doses plus faibles et peuvent entraîner une augmentation de l'incidence des symptômes extrapyramidaux. L'innocuité des doses supérieures à 16 mg/jour n'a pas été évaluée et n'est donc pas recommandée.
Âgé
Une dose initiale de 0,5 mg deux fois par jour est recommandée. Cette posologie peut être ajustée individuellement avec des augmentations de 0,5 mg deux fois par jour à 1 à 2 mg deux fois par jour.
Population pédiatrique
L'utilisation de la rispéridone n'est pas recommandée chez les enfants de moins de 18 ans atteints de schizophrénie en raison d'un manque de données sur son efficacité.

Effets indésirables:
Les effets indésirables les plus fréquemment rapportés associés à l'utilisation de l'olanzapine étaient la somnolence, la prise de poids, l'éosinophilie, les taux élevés de prolactine, de cholestérol, de glucose et de triglycérides, la glycosurie, l'augmentation de l'appétit, les étourdissements, l'akathisie, le parkinsonisme, la dyskinésie, l'hypotension orthostatique, les effets anticholinergiques, transitoires. élévations asymptomatiques des transaminases hépatiques, éruption cutanée, asthénie, fatigue et œdème.

Interactions médicamenteuses :
Médicaments connus pour allonger l'intervalle QT
Comme avec d'autres antipsychotiques, la prudence est recommandée lors de la prescription de rispéridone avec des médicaments connus pour allonger l'intervalle QT, tels que des antiarythmiques (p. (c'est-à-dire maprotiline), certains antihistaminiques, d'autres antipsychotiques, certains antipaludiques (c'est-à-dire quinine et méfloquine), et avec des médicaments provoquant un déséquilibre électrolytique (hypokaliémie, hypomagnésiémie), une bradycardie ou ceux qui inhibent le métabolisme hépatique de la rispéridone. Cette liste est indicative et non exhaustive.
Drogues et alcool à action centrale
La rispéridone doit être utilisée avec prudence en association avec d'autres substances à action centrale, notamment l'alcool, les opiacés, les antihistaminiques et les benzodiazépines en raison du risque accru de sédation.
Agonistes de la lévodopa et de la dopamine
Les comprimés de rispéridone peuvent antagoniser l'effet de la lévodopa et d'autres agonistes de la dopamine. Si cette association est jugée nécessaire, notamment au stade terminal de la maladie de Parkinson, la dose efficace la plus faible de chaque traitement doit être prescrite.
Médicaments à effet hypotenseur
Une hypotension cliniquement significative a été observée après commercialisation lors de l'utilisation concomitante de rispéridone et d'un traitement antihypertenseur.
Palipéridone
L'utilisation concomitante de comprimés de rispéridone par voie orale avec la palipéridone n'est pas recommandée car la palipéridone est le métabolite actif de la rispéridone et l'association des deux peut entraîner une exposition additive à la fraction antipsychotique active.

Grossesse et allaitement:
Grossesse
Il n'existe pas de données adéquates sur l'utilisation de la rispéridone chez la femme enceinte. La rispéridone n'a pas été tératogène dans les études animales, mais d'autres types de toxicité pour la reproduction ont été observés. Le risque potentiel pour l'homme est inconnu.
Les nouveau-nés exposés aux antipsychotiques (y compris les comprimés de rispéridone) au cours du troisième trimestre de la grossesse sont à risque de réactions indésirables, y compris des symptômes extrapyramidaux et/ou de sevrage qui peuvent varier en sévérité et en durée après l'accouchement. Des cas d'agitation, d'hypertonie, d'hypotonie, de tremblements, de somnolence, de détresse respiratoire ou de troubles de l'alimentation ont été rapportés. Par conséquent, les nouveau-nés doivent être surveillés attentivement.
Les comprimés de rispéridone ne doivent pas être utilisés pendant la grossesse, sauf en cas de nécessité absolue. Si l'arrêt pendant la grossesse est nécessaire, il ne doit pas être fait brutalement.
Allaitement maternel
Dans les études animales, la rispéridone et la 9-hydroxy-rispéridone sont excrétées dans le lait. Il a été démontré que la rispéridone et la 9-hydroxy-rispéridone sont également excrétées dans le lait maternel en petites quantités. Il n'y a pas de données disponibles sur les effets indésirables chez les nourrissons allaités. Par conséquent, l'avantage de l'allaitement doit être mis en balance avec les risques potentiels pour l'enfant.

Précaution/Avertissements :
- Patients âgés atteints de démence
- Augmentation de la mortalité chez les personnes âgées atteintes de démence
- Dans une méta-analyse de 17 essais contrôlés d'antipsychotiques atypiques, y compris les comprimés de rispéridone, les patients âgés atteints de démence traités par des antipsychotiques atypiques ont une mortalité accrue par rapport au placebo. Dans les essais contrôlés par placebo avec les comprimés de rispéridone par voie orale dans cette population, l'incidence de la mortalité était de 4,0 % pour les patients traités par comprimés de rispéridone par rapport à 3,1 % pour les patients traités par placebo. L'odds ratio (intervalle de confiance exact à 95 %) était de 1,21 (0,7, 2,1). L'âge moyen (intervalle) des patients décédés était de 86 ans (intervalle 67-100). Les données de deux grandes études observationnelles ont montré que les personnes âgées atteintes de démence qui sont traitées avec des antipsychotiques conventionnels courent également un risque légèrement accru de décès par rapport à celles qui ne sont pas traitées. Les données sont insuffisantes pour donner une estimation ferme de l'ampleur précise du risque et la cause de l'augmentation du risque n'est pas connue. La mesure dans laquelle les résultats d'une mortalité accrue dans les études d'observation peuvent être attribuées au médicament antipsychotique par opposition à certaines caractéristiques des patients n'est pas claire.
- Utilisation concomitante avec le furosémide
- Dans les essais contrôlés par placebo sur les comprimés de rispéridone chez des patients âgés atteints de démence, une incidence plus élevée de mortalité a été observée chez les patients traités par furosémide plus rispéridone (7,3 % ; âge moyen 89 ans, intervalle 75-97) par rapport aux patients traités par rispéridone seule. (3,1 % ; âge moyen 84 ans, intervalle 70-96) ou furosémide seul (4,1 % ; âge moyen 80 ans, intervalle 67-90). L'augmentation de la mortalité chez les patients traités par furosémide plus rispéridone a été observée dans deux des quatre essais cliniques. L'utilisation concomitante de rispéridone avec d'autres diurétiques (principalement des diurétiques thiazidiques utilisés à faible dose) n'a pas été associée à des résultats similaires.
- Aucun mécanisme physiopathologique n'a été identifié pour expliquer ce résultat, et aucun schéma cohérent de cause de décès n'a été observé. Néanmoins, des précautions doivent être prises et les risques et bénéfices de cette association ou d'un co-traitement avec d'autres diurétiques puissants doivent être pris en compte avant la décision d'utilisation. Il n'y a pas eu d'augmentation de l'incidence de la mortalité chez les patients prenant d'autres diurétiques en association avec la rispéridone. Quel que soit le traitement, la déshydratation était un facteur de risque global de mortalité et doit donc être soigneusement évitée chez les patients âgés atteints de démence.
- Événements indésirables cérébrovasculaires (EVAC)
- Un risque environ 3 fois plus élevé d'événements indésirables cérébrovasculaires a été observé dans des essais cliniques randomisés contrôlés par placebo dans la population atteinte de démence avec certains antipsychotiques atypiques. Les données regroupées de six études contrôlées par placebo avec les comprimés de rispéridone chez des patients principalement âgés (> 65 ans) atteints de démence ont montré que des AVC (graves et non graves, combinés) sont survenus chez 3,3 % (33/1009) des patients traités par rispéridone et 1,2 % (8/712) des patients traités par placebo. L'odds ratio (intervalle de confiance exact à 95 %) était de 2,96 (1,34, 7,50). Le mécanisme de ce risque accru n'est pas connu. Un risque accru ne peut être exclu pour d'autres antipsychotiques ou d'autres populations de patients. Les comprimés de rispéridone doivent être utilisés avec prudence chez les patients présentant des facteurs de risque d'AVC.
- Le risque d'AVC était significativement plus élevé chez les patients atteints de démence de type mixte ou vasculaire par rapport à la démence d'Alzheimer. Par conséquent, les patients atteints d'autres types de démence que la maladie d'Alzheimer ne doivent pas être traités par la rispéridone.
- Il est conseillé aux médecins d'évaluer les risques et les bénéfices de l'utilisation des comprimés de rispéridone chez les patients âgés atteints de démence, en tenant compte des facteurs prédictifs de risque d'accident vasculaire cérébral chez chaque patient. Les patients/soignants doivent être avertis de signaler immédiatement les signes et symptômes d'événements cardiovasculaires potentiels tels qu'une faiblesse soudaine ou un engourdissement du visage, des bras ou des jambes, et des problèmes d'élocution ou de vision. Toutes les options thérapeutiques doivent être envisagées sans délai, y compris l'arrêt de la rispéridone.
- Les comprimés de rispéridone ne doivent être utilisés qu'à court terme en cas d'agressivité persistante chez les patients atteints de démence d'Alzheimer modérée à sévère, en complément d'approches non pharmacologiques qui ont eu une efficacité limitée ou inexistante et lorsqu'il existe un risque potentiel d'atteinte à soi-même ou à autrui.

Surdosage et traitements :
Symptômes
En général, les signes et symptômes rapportés sont ceux résultant d'une exagération des effets pharmacologiques connus de la rispéridone. Ceux-ci incluent la somnolence et la sédation, la tachycardie et l'hypotension, et les symptômes extrapyramidaux. En cas de surdosage, un allongement de l'intervalle QT et des convulsions ont été rapportés. Des torsades de pointes ont été signalées en association avec un surdosage combiné de comprimés de rispéridone et de paroxétine.
En cas de surdosage aigu, la possibilité d'une implication multiple du médicament doit être envisagée.
Traitement
Établir et maintenir des voies respiratoires dégagées et assurer une oxygénation et une ventilation adéquates. Un lavage gastrique (après intubation, si le patient est inconscient) et l'administration de charbon activé avec un laxatif ne doivent être envisagés que lorsque la prise du médicament a eu lieu moins d'une heure avant. La surveillance cardiovasculaire doit commencer immédiatement et doit inclure une surveillance électrocardiographique continue pour détecter d'éventuelles arythmies.
Il n'y a pas d'antidote spécifique aux comprimés de rispéridone. Par conséquent, des mesures de soutien appropriées devraient être instituées. L'hypotension et le collapsus circulatoire doivent être traités par des mesures appropriées telles que des liquides intraveineux et/ou des agents sympathomimétiques. En cas de symptômes extrapyramidaux sévères, un médicament anticholinergique doit être administré. Une surveillance et une surveillance médicales étroites doivent se poursuivre jusqu'à ce que le patient se rétablisse.

Emballage : 3 x 10 Comprimés Alu-Alu Blister

Durée de conservation : 36 mois

Condition de stockage : Conserver dans un endroit frais et sec à l'abri de la lumière