PACKAGE INSERT FOR

RISNIA TABLETS

SCHEDULING STATUS:

S5

NAME OF THE MEDICINE:

RISNIA 0,5 mg (Tablets)

RISNIA 1 mg (Tablets)

RISNIA 2 mg (Tablets)

RISNIA 3 mg (Tablets)

RISNIA 4 mg (Tablets)

RISNIA 6 mg (Tablets)

QUALITATIVE AND QUANTITATIVE COMPOSITION

RISNIA 0,5 mg:

Each tablet contains risperidone 0,5 mg

Contains sugar: (Lactose monohydrate 69,20 mg)

RISNIA 1 mg:

Each tablet contains risperidone 1 mg

Contains sugar: (Lactose monohydrate 69,00 mg)

RISNIA 2 mg:

Each tablet contains risperidone 2 mg

Contains sugar: (Lactose monohydrate 138,00 mg)

RISNIA 3 mg:

Each tablet contains risperidone 3 mg

Contains sugar: (Lactose monohydrate 207,00 mg)

RISNIA 4 mg:

Each tablet contains risperidone 4 mg

Contains sugar: (Lactose monohydrate 276,00 mg)

RISNIA 6 mg:

Each tablet contains risperidone 6 mg

Contains sugar: (Lactose monohydrate 274,00 mg)

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM:

Tablets

RISNIA 0,5 mg: Brown coloured, circular, biconvex, film-coated tablets imprinted “0.5” on one side and plain on the other side.

RISNIA 1 mg: White, round, film-coated tablets imprinted “1” on one side and plain on the other side.

RISNIA 2 mg: Orange, round, film-coated tablets imprinted “2” on one side and plain on the other side.

RISNIA 3 mg: Yellow, round, film-coated tablets imprinted “3” on one side and plain on the other side.

RISNIA 4 mg: Green, round, film-coated tablets imprinted “4” on one side and plain on the other side.

RISNIA 6 mg: Yellow, capsule-shaped, biconvex, film-coated tablets imprinted “6” on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

RISNIA is indicated for the treatment of:

- Acute and chronic schizophrenic psychoses and related psychosis in which positive symptoms (such as hallucinations, delusions, thought disturbances, hostility, suspiciousness) and/or the negative symptoms (such as blunted affect, emotional and social withdrawal, poverty of speech) are prominent. RISNIA also alleviates affective symptoms (such as depression, guilt feelings, anxiety) associated with schizophrenia. In patients who have shown an initial treatment response, RISNIA is also effective in maintaining the clinical improvement.
- Mania in bipolar disorder. These episodes are characterised by symptoms such as elevated, expansive or irritable mood, inflated self-esteem, decreased need for sleep, pressured speech, racing thoughts, distractibility, or poor judgment, including disruptive or aggressive behaviours.
- Conduct and other disruptive behaviour disorders in children (aged 5 to 12 years), with subaverage intellectual functioning or mental retardation in whom destructive behaviours (e.g. aggression, impulsivity and self-injurious behaviours) are prominent.

4.2 Posology and method of administration

Adults:

RISNIA may be given once or twice daily.

Patients should start with 2 mg/day RISNIA. The dosage may be increased on the second day to 4 mg/day. From then on, the dosage can be maintained unchanged, or further individualised, if needed. Most patients will benefit from daily doses of between 4 mg/day and 8 mg/day. Doses above 6 mg/day (when administered twice daily) were associated with more extrapyramidal symptoms and other adverse effects and are not generally recommended. In some patients, particularly with first episode acute psychosis, a slower titration phase and a lower starting and maintenance dose may be appropriate.

Doses above 10 mg/day have not been shown to be superior in efficacy to lower doses and may cause an increased incidence of side-effects such as extrapyramidal symptoms. Dosages above 10 mg/day should only be considered. The maximum total daily dose is 16 mg/day.

Posology

Schizophrenia

Switching from other antipsychotics to RISNIA:

When medically appropriate, gradual discontinuation of the previous treatment, while RISNIA therapy is initiated, is recommended. Also if medically appropriate, when switching patients from depot antipsychotics, initiate RISNIA therapy in place of the next scheduled injection. The need for continuing existing anti-Parkinson medications should be re-evaluated periodically.

Mania in bipolar disorders

RISNIA should be administered on a once daily schedule, starting with 2 or 3 mg. Dosage

adjustments, if indicated, should occur at intervals of not less than 24 hours and in dosage increments of 1 mg per day. Efficacy was demonstrated in flexible doses over a range of 1 to 6 mg per day.

The continued use of RISNIA must be evaluated and justified on an ongoing basis.

Experience is lacking in bipolar mania in children and adolescents less than 18 years of age.

Special populations

Renal and liver impairment

Patients with renal impairment have less ability to eliminate the active antipsychotic fraction than normal adults. 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.

RISNIA should be used with caution in these groups of patients.

A benzodiazepine may be added to RISNIA if additional sedation is required.

Patients < 50 kg:

A starting dose of 0,01 mg/kg once daily is recommended. This dosage can be individually adjusted by increments of 0,01 mg/kg once daily not more frequently than every other day, if needed. The recommended maintenance dose is 0,02 to 0,04 mg/kg once daily. The mean dose is 0,03 mg/kg once daily.

The continued use of RISNIA must be evaluated and justified on an ongoing basis.

Experience is lacking in children aged less than 5 years.

Elderly patients and patients with renal and hepatic impairment.

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

Children:

The safety and efficacy of RISNIA in children aged under 15 years have not yet been established in schizophrenia.

Conduct and other Disruptive Behaviour Disorders (DBD) in children 5 to 12 years of age.

Method of administration:

Oral tablets for swallowing

4.3 Contraindications

RISNIA is contraindicated in:

- Patients with known hypersensitivity to risperidone or to any of the excipients in RISNIA (see **section 6.1**).
- Conduct and other disruptive behaviour disorders in children: RISNIA is contraindicated in children under 5 years of age as efficacy and safety in these children have not been demonstrated.
- Parkinson's disease and Lewy Body Dementia (see **section 4.4**).

4.4 Special warnings and precautions for use

Overall Mortality

As reported in studies, elderly patients with dementia treated with atypical antipsychotic medicines have an increased mortality compared to placebo in a meta-analysis of 17 controlled trials of atypical antipsychotic medicines, including risperidone. In placebo-

controlled trials with oral risperidone in this population, the incidence of mortality was 4,0 % for risperidone treated patients compared to 3,1 % for placebo-treated patients. The mean age (range) of patients who died was 86 years (range 67-100).

Concomitant use with furosemide

As reported in studies, placebo-controlled trials in elderly patients with dementia, a higher incidence of mortality was observed in patients treated with furosemide and risperidone (7,3 %; mean age 89 years, range 75 to 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 to 90). The increase in mortality in patients treated with furosemide plus risperidone was observed in two of the four clinical trials.

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 should be considered prior to the decision to use. There was no increased incidence of mortality among patients taking other diuretics as concomitant medication with RISNIA. 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 (CAE)

As reported, in placebo-controlled clinical trials in elderly patients with dementia, there was a higher incidence of cerebrovascular adverse events (cerebrovascular accidents and transient ischaemic attacks), including fatalities, in patients treated with RISNIA compared to patients receiving placebo (mean age 85 years; range 73 to 97 years).

Orthostatic Hypotension

Due to the alpha-blocking activity of RISNIA, (orthostatic) hypotension can occur, especially during the initial dose-titration period. RISNIA 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.

Leucopaenia, Neutropaenia, and Agranulocytosis

Events of leucopaenia, neutropaenia and agranulocytosis have been reported with RISNIA. Agranulocytosis has been reported during post-marketing surveillance.

Patients with a history of a clinically significant low white blood cell count (WBC) or a medicine-induced leucopaenia/neutropaenia should be monitored during therapy and discontinuation of RISNIA should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors.

Patients with clinically significant neutropaenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropaenia (absolute neutrophil count < 1 X 109/L) should discontinue RISNIA and have their WBC followed until recovery.

Venous thromboembolism

Cases of venous thromboembolism (VTE) have been reported with RISNIA. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with RISNIA and preventive measures undertaken.

Tardive Dyskinesia/Extrapyramidal Symptoms (TD/EPS)

RISNIA has been associated with the induction of tardive dyskinesia (TD) characterised by

potentially irreversible rhythmical involuntary movements, predominantly of the tongue and/or face. It has been reported that the occurrence of extrapyramidal symptoms is a risk factor for the development of tardive dyskinesia. TD appears to be most prominent in the elderly especially elderly females. If signs and symptoms of tardive dyskinesia appear, the discontinuation of RISNIA should be considered.

Neuroleptic Malignant Syndrome (NMS)

Neuroleptic Malignant Syndrome, a potentially fatal symptom complex, characterised by hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated serum creatine phosphokinase levels has been reported to occur in association with RISNIA. Additional signs may include elevated creatine phosphokinase levels, myoglobinuria (rhabdomyolysis) and acute renal failure. In this event, RISNIA, should be discontinued.

Parkinson's disease/Lewy Body dementia and NMS

Patients with Parkinson's disease or Dementia with Lewy Bodies (DLB) have an increased risk of Neuroleptic Malignant Syndrome (NMS) as well as having an increased sensitivity to antipsychotic medications (see CONTRAINDICATIONS). Manifestation of this increased sensitivity can include confusion, obtundation and postural instability with frequent falls, in addition to extrapyramidal symptoms. In addition, in clinical trials, elderly patients have a higher mortality than placebo treated elderly patients. (see CONTRAINDICATIONS).

Hyperglycaemia and diabetes mellitus

Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with RISNIA.

Patients with an established diagnosis of diabetes mellitus who are starting on RISNIA should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g. obesity, family history of diabetes) who are starting treatment with

RISNIA should be monitored for symptoms of hyperglycaemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycaemia during treatment with RISNIA should undergo fasting blood glucose testing. In some cases, hyperglycaemia has resolved when RISNIA were discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of RISNIA.

Weight gain

Significant weight gain has been reported. Monitoring weight gain is advisable when RISNIA is being used. Patients may be advised to refrain from excessive eating in view of the possibility of weight gain.

QT Interval

Caution should be exercised when RISNIA is prescribed in patients with a history of cardiac dysrhythmias, in patients with congenital long QT syndrome, and in concomitant use with medicines known to prolong the QT interval.

Priapism

Medicines with alpha-adrenergic blocking effects have been reported to induce priapism. Priapism has been reported with RISNIA during postmarketing surveillance (see **section 4.8**).

Body Temperature Regulation

Disruption of the body's ability to reduce core body temperature may occur. Appropriate care is advised when prescribing RISNIA to patients who will be experiencing conditions which may contribute to an elevation in core body temperature, e.g. exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration.

Antiemetic Effect

An antiemetic effect was observed in preclinical studies with risperidone. This effect, if it occurs in humans, may mask the signs and symptoms of overdosage with certain medicines or of conditions such as intestinal obstruction, Reye's syndrome, and brain tumour.

Intraoperative Floppy Iris Syndrome

Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in patients treated with medicines with alpha1a-adrenergic antagonist effect, including RISNIA.

IFIS may increase the risk of eye complications during and after the operation. Current or past use of RISNIA should be made known to the ophthalmic surgeon in advance of surgery. The potential benefit of stopping RISNIA prior to cataract surgery has not been established and must be weighed against the risk of stopping RISNIA therapy.

Seizures

RISNIA should be used cautiously in patients with a history of seizures or other conditions that potentially lower the seizure threshold.

Sugar/excipient name

RISNIA contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

There is increased mortality in elderly patients with dementia concomitantly receiving furosemide and RISNIA (see **section 4.4**).

The risk of using RISNIA in combination with other medicines has not been systematically

evaluated. Given the primary CNS depressive effects of RISNIA, it should be used with caution in combination with alcohol and other centrally acting medicines.

RISNIA may antagonise the effect of levodopa and other dopamine agonists.

Clinically significant hypotension has been observed postmarketing with concomitant use of RISNIA and antihypertensive treatment (see **section 4.4**).

Caution is advised when prescribing RISNIA with medicines known to prolong the QT interval (See **section 4.4**).

Carbamazepine has been shown to decrease the plasma levels of the active antipsychotic fraction of risperidone. Similar effects may be observed with other CYP3A4 hepatic enzyme inducers. On discontinuation of carbamazepine or other hepatic enzyme inducers, the dosage of RISNIA should be re-evaluated and, if necessary, decreased.

Fluoxetine and paroxetine, CYP 2D6 inhibitors, increase the plasma concentration of risperidone but less so of the active anti-psychotic fraction. When concomitant fluoxetine or paroxetine is initiated or discontinued, the dosing of RISNIA should be re-evaluated.

Venlafaxine administered under steady-state conditions at 150 mg/day inhibited the CYP2D6-mediated metabolism of risperidone (administered as a single 1 mg oral dose) to its active metabolite, 9-hydroxyrisperidone, resulting in an approximate 32 % increase in risperidone.

AUC. However, venlafaxine coadministration did not significantly alter the pharmacokinetic profile of the total active antipsychotic fraction.

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.

Phenothiazines, tricyclic antidepressants and some beta-blockers may increase the plasma concentration of risperidone but not that of the active antipsychotic fraction.

Amitriptyline does not affect the pharmacokinetics of risperidone or the active antipsychotic fraction. Cimetidine and ranitidine increased the bioavailability of risperidone, but only marginally that of the active antipsychotic fraction.

Erythromycin, a CYP 3A4 inhibitor, does not change the pharmacokinetics of risperidone and the active antipsychotic fraction.

The cholinesterase inhibitors, galantamine and donepezil, do not show a clinically relevant effect on the pharmacokinetics of risperidone and the active antipsychotic fraction.

When RISNIA is taken together with other highly protein-bound medicines (e.g. diazepam, warfarin, digoxin, imipramine and propranolol), there is no clinically relevant displacement of either agent from the plasma proteins.

RISNIA does not show a clinically relevant effect on the pharmacokinetics of lithium, valproate, digoxin or topiramate.

Food does not affect the absorption of RISNIA.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / Contraception in males and females

Not Applicable

The safety of RISNIA in pregnancy and lactating women has not been established.

Although, in experimental animals, risperidone did not show direct reproductive toxicity, some indirect, prolactin- and CNS-mediated effects were observed. No teratogenic effect of risperidone was noted in any study.

Neonates exposed to antipsychotic medicines (including RISNIA) during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms that may vary in severity following delivery. These symptoms in the neonates may include agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder.

Therefore, RISNIA should only be used during pregnancy.

Breastfeeding.

As reported 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. Therefore, women receiving RISNIA should not breastfeed.

Fertility

Not Applicable

4.7 Effects on ability to drive and use machines

RISNIA may impair mental alertness. Patients should therefore be advised not to drive or operate machinery until their individual susceptibility is known.

4.8 Undesirable effects

Tabulated list of adverse reactions

The adverse events considered at least possibly related to the treatment are listed below by body system organ class and frequency (wherever applicable).

MedDRA system organ class	Frequency	Side effects
Infections and infestations	Frequent	Pneumonia, influenza, bronchitis, upper respiratory tract infection, urinary tract infection
	Frequent	Sinusitis, viral infection, ear infection, tonsillitis, cellulitis, otitis media, eye infection, localised infection, acarodermatitis, respiratory tract infection, cystitis, onychomycosis
	Less Frequent	Otitis media chronic
Blood and lymphatic system disorders	Frequent	Anaemia, neutropaenia
	Less Frequent	Granulocytopaenia
Immune system disorders	Frequent	Hypersensitivity
	Less Frequent	Drug hypersensitivity
Metabolism and nutrition disorders	Frequent	Increased appetite, decreased appetite
	Frequent	Anorexia, polydipsia
Psychiatric disorders	Frequent	Insomnia
	Frequent	Anxiety, agitation, sleep disorder
	Frequent	Confusional state, decreased libido, listless, nervousness
	Less Frequent	Anorgasmia, blunted affect
Nervous system disorders	Frequent	Parkinsonism , headache
	Frequent	Akathisia , dizziness, tremor , dystonia , somnolence, sedation, lethargy, dyskinesia

	Frequent	Unresponsive to stimuli, loss of consciousness, syncope, depressed level of consciousness, cerebrovascular accident, transient ischaemic attack, dysarthria, disturbance in attention, hypersomnia, postural dizziness, balance disorder, tardive dyskinesia, speech disorder, coordination abnormal, hypoaesthesia, head titubation
	Less Frequent	Neuroleptic malignant syndrome, diabetic coma, cerebrovascular disorder, cerebral ischaemia, movement disorder
Eye disorder	Frequent	Blurred vision
	Frequent	Conjunctivitis, ocular hyperaemia, eye discharge, eye swelling, dry eye, increased lacrimation, photophobia
	Less Frequent	Reduced visual acuity, eye rolling, glaucoma
Ear and labyrinth disorders	Frequent	Ear pain, tinnitus
Cardiac disorders	Frequent	Tachycardia
	Frequent	Atrioventricular block, bundle branch block, sinus bradycardia, palpitations
Vascular disorders	Frequent	Hypotension, orthostatic hypotension, flushing
Respiratory, thoracic and mediastinal disorders	Frequent	Dyspnoea, epistaxis, cough, nasal congestion, pharyngolaryngeal pain
	Frequent	Wheezing, pneumonia aspiration, pulmonary congestion, respiratory disorder, rales, respiratory tract congestion, dysphonia
	Less Frequent	Hyperventilation

Gastrointestinal disorders	Frequent	Vomiting, diarrhoea, constipation, nausea, abdominal pain, dyspepsia, dry mouth, stomach discomfort
	Frequent	Dysphagia, gastritis, faecal incontinence, faecaloma
	Less Frequent	Lip swelling, cheilitis
Skin and subcutaneous tissue disorders	Frequent	Rash, erythema
	Frequent	Skin lesion, skin disorder, pruritus, acne, skin discolouration, seborrhoeic dermatitis, dry skin, hyperkeratosis
	Rare	Dandruff
Musculoskeletal and connective tissue disorders	Frequent	Arthralgia, back pain, pain in extremity
	Frequent	Muscular weakness, myalgia, neck pain, joint swelling, posture abnormal, joint stiffness, musculoskeletal chest pain
	Less Frequent	Rhabdomyolysis
Renal and urinary disorders	Frequent	Enuresis
	Frequent	Dysuria, urinary incontinence, pollakiuria
Reproductive system and breast disorders	Frequent	Amenorrhoea, sexual dysfunction, erectile dysfunction, ejaculation disorder, galactorrhoea, gynaecomastia, menstrual disorder, vaginal discharge
General disorders and administration site conditions	Frequent	Pyrexia, fatigue, peripheral oedema, asthenia, chest pain
	Frequent	Face oedema, gait disturbance, feeling abnormal, sluggishness, influenza like illness, thirst, chest discomfort, chills
	Less Frequent	Generalised oedema, drug withdrawal syndrome, peripheral coldness
Investigations	Frequent	Increased blood prolactin, increased weight

	Frequent	Abnormal electrocardiogram, increased blood glucose, increased transaminases, decreased white blood cell count, increased body temperature, increased eosinophil count, decreased haemoglobin, increased blood creatine phosphokinase
	Less Frequent	Decreased body temperature

Post-marketing adverse events

System organ class	**Side effect**
Blood and lymphatic system disorders	Thrombocytopaenia, agranulocytosis
Immune system disorder	Anaphylactic reaction, angioedema
Endocrine disorder	Inappropriate antidiuretic hormone secretion
Metabolism and nutrition disorder	Diabetic ketoacidosis, water intoxication, diabetes mellitus, hypoglycaemia, increased blood cholesterol, increased blood triglycerides
Psychiatric disorder	Mania
Nervous System Disorder	Dysgeusia
Eye Disorders	Floppy iris syndrome (intraoperative)
Cardiac disorders	Atrial fibrillation
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome
Gastro-intestinal disorders	Intestinal obstruction, pancreatitis, paralytic ileus
Hepatobiliary disorders	Jaundice
Skin and subcutaneous tissue disorder	Alopecia
Renal and urinary disorders	Urinary retention
Pregnancy, Puerperium and Perinatal Conditions	Neonatal drug withdrawal syndrome
Reproductive system and breast disorders	Priapism

General disorders	Hypothermia
Investigations	Electrocardiogram QT prolongation

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website, or to Cipla Medpro (Pty) Ltd. by email: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

4.9 Overdose

Reported signs and symptoms have been those resulting from an exaggeration of the medicine's known pharmacological effects. Symptoms of acute overdosage include drowsiness, sedation, hypotension, tachycardia and extrapyramidal symptoms. In overdose, cases of QT-prolongation have been reported.

In the case of acute overdosage, the possibility of multiple medicine ingestion should be considered.

Treatment:

Establish and maintain a clear airway and ensure adequate oxygenation and ventilation. (after intubation, if the patient is unconscious) and administration of activated charcoal together with a laxative should be considered. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible dysrhythmias.

Since there is no known antidote if accidental poisoning or overdosage is suspected,

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, anticholinergic medication should be administered. Close medical supervision and monitoring should continue until the patient recovers.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A.2.6.5

Pharmacotherapeutic group: Central nervous system depressants. Miscellaneous structures

ATC code: N05AX08

Mechanism of action

Pharmacodynamic effects:

Risperidone is anantipsychotic of the benzisoxazol derivatives. It is a selective monoaminergic antagonist. Risperidone has affinity for serotonin-5-HT2, dopamine-D2, H1-histamine, alpha1- and alpha2-adrenergic receptors. Risperidone has no affinity for cholinergic receptors. It is a dopamine D2-antagonist.

Clinical efficacy and safety:

Not Applicable

5.2 Pharmacokinetic properties

Absorption

Risperidone is completely absorbed after oral administration. Peak plasma concentrations are attained within 1 to 2 hours. Food does not affect the absorption of risperidone.

Distribution

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 4 mg twice daily.

Steady state is reached within 1 day for risperidone in most patients and 4 to 5 days for 9-hydroxy-risperidone.

Biotransformation

Risperidone is metabolised by cytochrome CYP 2D6 to 9-hydroxy-risperidone, which has a similar pharmacological activity to risperidone. Risperidone and 9-hydroxy-risperidone form the active antipsychotic fraction.

Elimination

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.

Linearity/non-linearity

Risperidone plasma concentration is dose-proportional within the therapeutic dose-range. Risperidone 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 to 45 % of the dose.

Risperidone showed higher active plasma concentrations and a reduced clearance of the active antipsychotic fraction by 30 % in the elderly and 50 % in patients with moderate renal insufficiency. In patients with severe renal insufficiency the clearance was one third that of normal. The plasma concentrations of risperidone were normal in patients with liver insufficiency, but the mean free fraction of risperidone in plasma was increased by about 35

%.

The pharmacokinetics of risperidone, 9-hydroxy-risperidone and the active moiety in children are similar to those in adults.

5.3 Preclinical safety data

Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

Corn starch

Microcrystalline cellulose

Sodium starch glycollate

Red oxide of iron

Magnesium stearate

Coating Material

Opadry 03B56826 brown

Opadry 03B58807 white

Opadry 03B53353 orange

Opadry 03B52319 yellow

Opadry 03B51168 green

Opacode S-1-815HV black

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 ºC.

Keep the blisters in the outer carton until required for use.

6.5 Nature and contents of container

RISNIA 0,5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 6 mg are packed in PVC/PE/PVDC film Blister strips of 10 tablets in a carton.

Pack sizes: Blister strips of 10 tablets, packed in 30’s

6.6 Special precautions for disposal and other handling

No special requirements.

8. REGISTRATION NUMBER(S):

RISNIA 0,5 mg: 42/2.6.5/0792

RISNIA 1 mg: 42/2.6.5/0793

RISNIA 2 mg: 42/2.6.5/0794

RISNIA 3 mg: 42/2.6.5/0795

RISNIA 4 mg: 42/2.6.5/0796

RISNIA 6 mg: 42/2.6.5/0797

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorisation: 07 June 2012

Latest renewal: Not Applicable

10. DATE OF REVISION OF THE TEXT

06 July 2026