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CLINICAL APPROVAL LETTER: POST REGISTRATION APPLICATIONS

Clinical approval date	29-May-2026
Applicant's cover letter date	08-December-2025
Applicant	Unimed Healthcare (Pty) Ltd
Proprietary name(s) (including duplicates)	PMI RISPERIDONE 1 mg/ml
API(s)	Respiridone
Registration number(s)	43/2.6.5/0691
Sequence no	0013

Dear Sir/Madam,

Kindly be informed that the Authority has completed the evaluation of the above-mentioned Professional Information (PI) and Patient Information Leaflet (PIL) variation application.

1. The amendments to the PI and PIL are approved.
2. The PI and PIL be accepted as the currently approved PI and PIL
3. The date of revision reflected on this PI and PIL should be: **29-May-2026**
4. The final dated version of the above PI and PIL must be submitted via docubridge in a closing sequence using the Sequence Type "Closing sequence" and Sequence Description "Approved " updated PI and PIL within 10 working days.
5. The approved PI and PIL must be uploaded into the SAHPRA repository within 10 working days.

Note to applicant: Amendments to any quality aspects of the medicine within the PI and PIL are subject to P&A unit approval and may only be implemented in the PI if approved by the P&A unit.

Yours Faithfully,

Luleka Dhlamini

L.DHLAMINI

MANAGER: CLINICAL POST-REGISTRATION UNIT

PROFESSIONAL INFORMATION

SCHEDULING STATUS: S5

1. NAME OF THE MEDICINE

PMI RISPERIDONE 1 mg/ml (Oral Solution)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of the oral Solution contains 1 mg risperidone.

Preservative: Benzoic acid 0,15 % m/v

Sugar free

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Clear colourless solution free from foreign particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

PMI RISPERIDONE 1 mg/ml is indicated for:

- 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. PMI RISPERIDONE 1 mg/ml also alleviates affective symptoms (such as depression, guilt feelings, anxiety) associated with schizophrenia. In patients who have shown an initial treatment response, PMI RISPERIDONE 1 mg/ml is also effective in maintaining the clinical improvement.

- Behavioural disturbances in patients with dementia in whom symptoms such as aggressiveness, activity disturbances or psychotic symptoms are prominent.
- 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 – 12 years), with subaverage intellectual functioning or mental retardation in whom destructive behaviours are prominent.

4.2 Posology and method of administration

Schizophrenia:

Switching from other antipsychotics to PMI RISPERIDONE 1 mg/ml

When switching patients from depot antipsychotics, initiate PMI RISPERIDONE 1 mg/ml therapy in place of the next scheduled injection. The need for continuing existing medically appropriate, gradual discontinuation of the previous treatment is recommended. Also, if medically appropriate anti-Parkinson medications should be re-evaluated periodically.

Adults

PMI RISPERIDONE 1 mg/ml may be given on either a once a day or twice a day schedule.

Patients should start with 2 mg/day PMI RISPERIDONE 1 mg/ml; this may be increase to 4 mg/day on the second 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 to 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 if the benefits outweigh the risk. The maximum total daily dose is 16 mg/day. A benzodiazepine may be added to PMI RISPERIDONE 1 mg/ml if additional sedation is required.

***Hepatic and renal function impairment*:**

Clinical experience is lacking in these patient populations and PMI RISPERIDONE 1 mg/ml should therefore be administered with caution. 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. It is recommended to halve both the starting dose and the subsequent dose increments and dose titration should be slower for patients with renal or hepatic impairment.

Elderly patients

A starting dose of 0,5 mg twice daily is recommended. The dose can be individually adjusted with increments of 0,5 mg twice daily to 1 – 2 mg twice daily.

Children

Not for children under 15 years as efficacy and safety in children under the age of 15 have not been demonstrated in schizophrenia.

Mania in bipolar disorders

PMI RISPERIDONE 1 mg/ml 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 PMI RISPERIDONE 1 mg/ml 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.

Behavioural disturbances in patients with dementia:

A starting dose of 0,25 mg twice daily is recommended. This dosage can be individually increased 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. However, some patients may benefit from doses up to 1 mg twice daily. Once patients have reached their target dose, a once-daily dosing regimen can be considered. The continued use of PMI RISPERIDONE 1 mg/ml must be evaluated and justified on an ongoing basis.

Conduct and other disruptive behaviour disorders in children 5 – 12 years of age:

Subjects < 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 – 0,04 mg/kg once daily. The mean dose is 0,03 mg/kg once daily. The continued use of PMI RISPERIDONE 1 mg/ml must be evaluated and justified on an ongoing basis.

Experience is lacking in children under the age of 5 years.

Method of administration

PMI RISPERIDONE 1 mg/ml is for oral use. Food does not affect the absorption of risperidone.

4.3 Contraindications

- Hypersensitivity to risperidone or any of the excipients listed in section 6.1.
- Conduct and other disruptive behaviour disorders in children: PMI RISPERIDONE 1 mg/ml is contra-indicated in children under 5 years as efficacy and safety in children under the age of 5 years have not been established.
- Parkinson's disease and Lewy body dementia (see section 4.4).
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4.4 Special warnings and precautions for use

Elderly patients with dementia (see section 4.5)

Before prescribing, medical practitioners are advised to carefully assess the risks and benefits of the use of atypical antipsychotics in elderly patients with dementia, taking into account risk predictions for stroke in the individual patient (e.g. hypertension, diabetes, current smoking, atrial fibrillation, and age > 80 years).

Where the use of antipsychotics in the elderly is considered essential, the lowest effective dose should be used. These patients should be carefully monitored to avoid or reduce hypotension, gait disturbances, oversedation and complications associated with hyperglycaemia.

Risperidone, such as in PMI RISPERIDONE 1 mg/ml is not indicated in elderly patients with dementia exhibiting behavioural disturbances.

Increased mortality in elderly people with dementia

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 to 100).

Hepatic and Renal Impairment

In patients with severe hepatic impairment and renal function metabolism, excretion and protein binding of PMI RISPERIDONE 1 mg/ml may be decreased; reduced dosage is recommended (see section 4.2).

Tardive dyskinesia / extrapyramidal symptoms (TD/EPS)

Tardive dyskinesia (TD), a syndrome consisting of potentially irreversible, rhythmical involuntary dyskinetic movements predominantly of the tongue and/or face, may develop in patients treated with PMI RISPERIDONE 1 mg/ml. Although this syndrome of TD appears to be most prevalent in the elderly, especially elderly females, it is impossible to predict at the onset of treatment which patients are likely to develop TD.

The occurrence of extrapyramidal symptoms may be a predictor for the development of TD.

The risk of developing TD and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of the antipsychotic administered to the patient increase. However, the syndrome can develop, although less commonly, after relatively brief periods of treatment at low doses. There is no known treatment for an established case of TD. The syndrome may remit partially or completely if the antipsychotic medicine treatment is withdrawn.

PMI RISPERIDONE 1 mg/ml treatment itself, however, may suppress the signs and symptoms of TD, thereby masking the underlying process. The effect of symptom suppression upon the long-term course of TD is unknown. In view of these considerations, PMI RISPERIDONE 1 mg/ml should be prescribed in a manner that is most likely to minimise the risk of TD. PMI RISPERIDONE 1 mg/ml should be reserved for patients who appear to be obtaining substantial benefit from the medicine. In such patients the smallest dose and the shortest duration of treatment should be sought. The benefit for continued treatment should be reassessed periodically. If signs and symptoms of TD appear in a patient on antipsychotics,

PMI RISPERIDONE 1 mg/ml discontinuation should be considered. However, some patients may require treatment despite the presence of this syndrome.

Neuroleptic Malignant Syndrome

Neuroleptic Malignant Syndrome (NMS) is a potentially fatal symptom complex that has been reported in association with the use of PMI RISPERIDONE 1 mg/ml. Clinical manifestations of NMS are hyperthermia, muscle rigidity, altered mental status (including catatonic signs), evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, cardiac arrhythmias and diaphoresis) and elevated serum creatine phosphokinase levels.

Additional signs may include elevated creatine phosphokinase (CPK) levels, myoglobinuria (rhabdomyolysis), and acute renal failure. In this event, PMI RISPERIDONE 1 mg/ml should be discontinued.

Important considerations in the differential diagnosis of NMS include:

- Central anticholinergic toxicity, heat stroke, medicine fever and primary central nervous system pathology.
- Identifying cases where the clinical presentation includes both serious medical illnesses (e.g. pneumonia, systemic infection etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS).

The management of NMS should include:

1. Immediate discontinuation of all antipsychotic medicines and other drugs not essential to concurrent therapy;
2. Intensive symptomatic treatment and medical monitoring; and
3. Treatment of any concomitant serious medical problems for which treatments are available.

There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic medicine treatment after recovery of NMS, the potential reintroduction of medicine therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

A dose-dependent increase in plasma prolactin concentration may occur. Possible associated manifestations are: galactorrhoea, gynaecomastia, disturbances of the menstrual cycle and amenorrhoea. Premenopausal women who develop secondary amenorrhoea of greater than six months duration should receive appropriate preventative therapy to avoid hypo-oestrogenic bone loss. The risk-benefit should be considered when the patient has breast cancer as prolactin-dependent cancer may be exacerbated.

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 section 4.3). 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 were shown to have a higher mortality than placebo treated elderly patients (see section 4.3).

PMI RISPERIDONE 1 mg/ml may antagonise the effect of levodopa and other dopamine agonists.

Concomitant use with furosemide

In risperidone placebo-controlled trials in elderly patients with dementia, there was a higher mortality in patients treated with furosemide and risperidone when compared to patients treated with risperidone alone. 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. There was no increased incidence of mortality among patients taking other diuretics as concomitant medicine with risperidone. Caution is advised in patients treated with furosemide and risperidone, such as in PMI RISPERIDONE 1 mg/ml due to possible dehydration (see section 4.5). Dehydration was an overall risk factor for mortality and should therefore be carefully avoided in elderly patients with dementia.

Hyperglycaemia and diabetes mellitus

Hyperglycaemia, in some cases extreme and associated with ketoacidosis and hyperosmolar coma or death, has been reported in patients treated with PMI RISPERIDONE 1 mg/ml. Patients with an established diagnosis

of diabetes mellitus who are started on PMI RISPERIDONE 1 mg/ml 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 PMI RISPERIDONE 1 mg/ml should be monitored for symptoms of hyperglycaemia including polydipsia, polyuria, polyphagia and weakness. Patients who develop symptoms of hyperglycaemia during treatment with PMI RISPERIDONE 1 mg/ml should undergo fasting blood glucose testing. In some cases, hyperglycaemia has resolved when PMI RISPERIDONE 1 mg/ml was discontinued. However, some patients required continuation of anti-diabetic treatment despite discontinuation of PMI RISPERIDONE 1 mg/ml.

Cerebrovascular Adverse Events

Cerebrovascular adverse events (CAE), including cerebrovascular accidents and transient ischaemic attacks, have been reported during treatment with PMI RISPERIDONE 1 mg/ml.

In placebo-controlled clinical trials in elderly patients with dementia, there was a higher incidence of cerebrovascular adverse events, including cerebrovascular accidents and transient ischaemic attacks, in patients treated with risperidone compared to patients receiving placebo (mean age 85 years; range 73 – 97 years). Caution is also recommended in patients with a history of developing cerebrovascular disease.

Orthostatic hypotension

Due to the alpha-blocking activity of risperidone such as in PMI RISPERIDONE 1 mg/ml, (orthostatic) hypotension can occur, especially during the initial dose-titration period. PMI RISPERIDONE 1 mg/ml 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.

Seizures

Seizures have been reported after treatment with PMI RISPERIDONE 1 mg/ml. Caution is recommended when treating patients with epilepsy, a history of seizures or other conditions that potentially lower the seizure threshold.

Weight gain

Significant weight gain has been reported. Monitoring weight gain is advisable when PMI RISPERIDONE 1 mg/ml is being used. Patients should refrain from excessive eating in view of the possibility of weight gain.

Antiemetic effect

PMI RISPERIDONE 1 mg/ml antiemetic effect may mask signs and symptoms of the following conditions: brain tumour, intestinal obstruction, medication overdose or Reye's syndrome.

Leukopenia, Neutropenia, and Agranulocytosis

Events of leukopenia, neutropenia and agranulocytosis have been reported with PMI RISPERIDONE 1 mg/ml. 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 leukopenia/neutropenia should be monitored during therapy and discontinuation of PMI RISPERIDONE 1 mg/ml 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 neutropenia 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 neutropenia (absolute neutrophil count < 1 X 10^9/L) should discontinue PMI RISPERIDONE 1 mg/ml and have their WBC followed until recovery.

Venous thromboembolism

Cases of venous thromboembolism (VTE) have been reported with PMI RISPERIDONE 1 mg/ml. 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 PMI RISPERIDONE 1 mg/ml and preventive measures undertaken.

Hyperprolactinaemia

Hyperprolactinaemia is a common side effect of treatment with risperidone as in PMI RISPERIDONE 1 mg/ml. Evaluation of the prolactin plasma level is recommended in patients with evidence of possible prolactin-related side effects (e.g., gynaecomastia, menstrual disorders, anovulation, fertility disorder, decreased libido, erectile dysfunction, and galactorrhoea).

Tissue culture studies suggest that cell growth in human breast tumours may be stimulated by prolactin. Although no clear association with the administration of antipsychotics has so far been demonstrated in clinical and epidemiological studies, caution is recommended in patients with relevant medical history.

PMI RISPERIDONE 1 mg/ml should be used with caution in patients with pre-existing hyperprolactinaemia and in patients with possible prolactin-dependent tumours.

QT Interval

Caution should be exercised when PMI RISPERIDONE 1 mg/ml 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 PMI RISPERIDONE 1 mg/ml during post marketing 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 PMI RISPERIDONE 1 mg/ml 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.

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 PMI RISPERIDONE 1 mg/ml. IFIS may increase the risk of eye complications during and after the operation. Current or past use of PMI RISPERIDONE 1 mg/ml should be made known to the ophthalmic surgeon in advance of surgery. The potential benefit of stopping PMI RISPERIDONE 1 mg/ml prior to cataract surgery has not been established and must be weighed against the risk of stopping PMI RISPERIDONE 1 mg/ml therapy.

Children and adolescents

Before PMI RISPERIDONE 1 mg/ml is prescribed to a child or adolescent with conduct disorder they should be fully assessed for physical and social causes of the aggressive behaviour such as pain or inappropriate environmental demands.

The sedative effect of PMI RISPERIDONE 1 mg/ml should be closely monitored in this population because of possible consequences on learning ability. A change in the time of administration of PMI RISPERIDONE 1 mg/ml could improve the impact of the sedation on attention faculties of children and adolescents.

Risperidone, as in PMI RISPERIDONE 1 mg/ml was associated with mean increases in body weight and body mass index (BMI). Baseline weight measurement prior to treatment and regular weight monitoring are recommended. Changes in height in the long-term open-label extension studies were within expected age-appropriate norms. The effect of long-term risperidone treatment on sexual maturation and height has not been adequately studied.

Because of the potential effects of prolonged hyperprolactinemia on growth and sexual maturation in children and adolescents, regular clinical evaluation of endocrinological status should be considered, including measurements of height, weight, sexual maturation, monitoring of menstrual functioning, and other potential prolactin-related effects.

Results from a small post-marketing observational study showed that risperidone-exposed subjects between the ages of 8 to 16 years were on average approximately 3,0 to 4,8 cm taller than those who received other atypical antipsychotic medicines. This study was not adequate to determine whether exposure to risperidone had any impact on final adult height, or whether the result was due to a direct effect of risperidone on bone growth, or the effect of the underlying disease itself on bone growth, or the result of better control of the underlying disease with resulting increase in linear growth.

During treatment with risperidone, as in PMI RISPERIDONE 1 mg/ml regular examination for extrapyramidal symptoms and other movement disorders should also be conducted.

Excipients

This medicinal product contains 1,50 mg benzoic acid in each ml solution. Benzoic acid may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

4.5. Interaction with other medicines and other forms of interaction

The risk of using PMI RISPERIDONE 1 mg/ml in combination with other medicines has not been systematically evaluated.

Pharmacodynamic-related interactions

Medicines known to prolong the QT interval

Caution is advised when prescribing risperidone with medicines known to prolong the QT-interval, such as antidysrhythmics (e.g., quinidine, disopyramide, 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, hypomagnesaemia), bradycardia, or those which inhibit the hepatic metabolism of risperidone. This list is indicative and not exhaustive.

Centrally acting medicines and alcohol

Risperidone as in PMI RISPERIDONE 1 mg/ml 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 as in PMI RISPERIDONE 1 mg/ml 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.

Psychostimulants

The combined use of psychostimulants (e.g. methylphenidate) with risperidone as in PMI RISPERIDONE 1 mg/ml can lead to extrapyramidal symptoms upon change of either or both treatments (see section 4.4).

Medicines with hypotensive effect

Clinically significant hypotension has been observed post-marketing with concomitant use of risperidone as in PMI RISPERIDONE 1 mg/ml and antihypertensive treatment.

Paliperidone

Concomitant use of oral risperidone as in PMI RISPERIDONE 1 mg/ml 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.

Risperidone is mainly metabolised through CYP2D6, and to a lesser extent through CYP3A4. Both risperidone and its active metabolite 9-hydroxyrisperidone 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 as in PMI RISPERIDONE 1 mg/ml 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 CYP2D6 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 medical practitioner should re-evaluate the dosing of PMI RISPERIDONE 1 mg/ml.

CYP3A4 and/or P-gp inhibitors

Co-administration of risperidone as in PMI RISPERIDONE 1 mg/ml 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 medical practitioner should re-evaluate the dosing of PMI RISPERIDONE 1 mg/ml.

CYP3A4 and/or P-gp inducers

Co-administration of risperidone 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 medical practitioner should re-evaluate the dosing of PMI RISPERIDONE 1 mg/ml. 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 medicines

When risperidone as in PMI RISPERIDONE 1 mg/ml is taken together with highly protein-bound medicines, there is no clinically relevant displacement of either medicine from the plasma proteins.

When using concomitant medicines, 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 as in PMI RISPERIDONE 1 mg/ml in children and adolescents did not alter the pharmacokinetics and efficacy of risperidone.

Effect of other medicines on the pharmacokinetics of risperidone

Antibacterials

- Erythromycin, a moderate CYP3A4 inhibitor and P-gp inhibitor, does not change the pharmacokinetics of risperidone as in PMI RISPERIDONE 1 mg/ml 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 substrates, 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 (phenobarbitone), which also induce CYP3A4 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 200 mg/day increased the plasma concentrations of risperidone and decreased the plasma concentrations of 9-hydroxyrisperidone.

Antipsychotics

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

Chronic administration of clozapine may decrease the clearance of PMI RISPERIDONE 1 mg/ml resulting in increased plasma levels.

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 medicines

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. When either fluoxetine is initiated or discontinued; the doctor should re-evaluate the PMI RISPERIDONE 1 mg/ml dosing.
- 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. When paroxetine is initiated or discontinued; the doctor should re-evaluate the PMI RISPERIDONE 1 mg/ml dosing.

- Venlafaxine administered under steady state conditions at 150 mg/day inhibited theCYP2D6-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 co-administration did not significantly alter the pharmacokinetic profile of the total 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 than100 mg/day of sertraline or fluvoxamine may elevate concentrations of the risperidone active antipsychotic fraction.

Effect of risperidone on the pharmacokinetics of other medicines

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.

Digoxin

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.

Concomitant use of PMI RISPERIDONE 1 mg/ml with furosemide

There is increased mortality in elderly patients with dementia concomitantly receiving furosemide and risperidone as in PMI RISPERIDONE 1 mg/ml (see section 4.4).

4.6 Fertility, pregnancy and lactation

Safety of PMI RISPERIDONE 1 mg/ml in pregnancy or lactating women has not been established.

Pregnancy

Neonates exposed to antipsychotic medicines (including risperidone) 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.

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.

Breastfeeding

Risperidone and 9-hydroxyrisperidone are excreted in human breast milk. Therefore, women receiving PMI RISPERIDONE 1 mg/ml should not breastfeed.

Fertility

As with other drugs that antagonize dopamine D2 receptors, risperidone elevates prolactin levels. Hyperprolactinaemia 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.

4.7 Effects on ability to drive and use machines

PMI RISPERIDONE 1 mg/ml may impair mental alertness and therefore patients should be advised not to operate machinery or drive until their individual susceptibility has been determined.

4.8 Undesirable effects

In some instances, it has been difficult to differentiate adverse events from symptoms of the underlying psychosis.

Summary of the safety profile

The most frequently reported adverse drug reactions (ADRs) are parkinsonism, sedation/somnolence, headache, and insomnia.

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

Tabulated list of adverse reactions

Table 1: Tabulated list of adverse reactions		
System Organ Class	**Adverse reactions**	**Frequency**
Infections and infestations	Pneumonia, influenza, bronchitis, upper respiratory tract infection, sinusitis, urinary tract infection, ear infection	*Frequent*
	Viral infection, tonsillitis, cellulitis, otitis media, eye infection, localised infections, acarodermatitis, respiratory tract infection, cystitis, onychomycosis, chronic otitis media	*Less frequent*
Blood and lymphatic system disorders	Thrombocytopenic purpura, neutropenia, thrombocytopenia, anaemia, granulocytopenia, white blood cell counts decreased, haematocrit decreased, eosinophil count increased, agranulocytosis	*Less frequent*
Immune system disorders	Hypersensitivity, anaphylactic reaction, angioedema	*Less frequent*
	Medicine hypersensitivity	*Frequency unknown*
Endocrine disorders	Hyperprolactinaemia (which can in some cases lead to gynaecomastia, menstrual disturbances, amenorrhoea, anovulation, galactorrhoea, fertility disorder, decreased libido, erectile dysfunction)	*Frequent*
	Inappropriate secretion of the antidiuretic hormone (SIADH), glucose urine present	*Less frequent*
Metabolism and nutrition disorders	Weight increased, increased appetite, decreased appetite	*Frequent*
	Diabetes mellitus, hyperglycaemia and exacerbation or pre-existing diabetes mellitus, polydipsia, weight decreased, anorexia, blood cholesterol increased, water intoxication,	*Less frequent*

	hypoglycaemia, hyperinsulinemia, blood triglycerides increased, diabetic ketoacidosis	
Psychiatric disorders	Mood or mental changes, including aggressive behaviour, agitation, difficulty in concentration and memory problems, insomnia [(1)], depression, sleep disorder, anxiety	*Frequent*
	Mania or hypomania, confused state, decreased libido, listless, anorgasmia, blunted effect, mania, nightmare, catatonia, somnambulism, sleep related eating disorder, nervousness	*Less frequent*
Nervous system disorders	Akathisia [(1)]; dizziness; dystonia[(1)]; parkinsonism[(1)]; somnolence; asthenia; fatigue; lassitude; drowsiness; sedation/ somnolence; headache; increased dream activity; increased duration of sleep; dyskinesia[(1)], tremor	*Frequent*
	Hyper- or hypothermia; tardive dyskinesia (see section 4.4); neuroleptic malignant syndrome (NMS) (see section 4.4); polydipsia; seizure; tardive dystonia, cerebrovascular accident, cerebral ischaemia, unresponsive to stimuli, loss of consciousness, depressed level of consciousness, transient ischaemic attack, convulsion[(1)], syncope, psychomotor hyperactivity, balance disorder, coordination abnormal, dizziness postural, disturbance in attention, dysarthria, dysgeusia, hypoaesthesia, paraesthesia, cerebrovascular disorder, diabetic coma, head intubation	*Less frequent*
Eye disorders	Changes in vision (including disturbances of accommodation and blurred vision), conjunctivitis	*Frequent*
	Ocular hyperaemia, eye discharge, eye swelling, dry eye, lacrimation increased, photophobia, glaucoma, eye movement	*Less frequent*

	disorder, eye rolling, eyelid margin crusting, floppy iris syndrome (intraoperative)	
	Visual acuity reduced	*Frequency unknown*
Ear and labyrinth disorders	Ear pain, tinnitus, vertigo	*Less frequent*
Cardiac disorders	Tachycardia	*Frequent*
	Atrioventricular block, bundle branch block, sinus bradycardia, palpitations, atrial fibrillation, conduction disorder, electrocardiogram QT prolonged, bradycardia, electrocardiogram abnormal, sinus dysrrhythmia	*Less frequent*
Vascular disorder	Hypertension	*Frequent*
	Hypotension, orthostatic hypotension, flushing, pulmonary embolism, venous thrombosis	*Less frequent*
Respiratory, thoracic and mediastinal disorders	Dyspnoea; cough; pharyngitis; rhinitis; epistaxis, pharyngolaryngeal pain, nasal congestion	*Frequent*:
	Pneumonia aspiration, pulmonary congestion, respiratory tract congestion, rales, wheezing, dysphonia, respiratory disorder, sleep apnoea syndrome, hyperventilation	*Less frequent*
Gastrointestinal disorders	Constipation, diarrhoea; dyspepsia; vomiting; nausea, abdominal pain, dry mouth, abdominal discomfort, toothache	*Frequent*:
	Dysphagia, gastritis, faecal incontinence, faecaloma, flatulence, pancreatitis, intestinal obstruction, swollen tongue, cheilitis, gastroenteritis, ileus	*Less frequent*
Hepato-biliary disorders	Transaminases increased, gamma-glutamyltransferase increased, hepatic enzyme increased, jaundice	Less frequent
	Skin rash or itching, erythema	*Frequent*:

Skin and subcutaneous tissue disorders	Dry skin; increased pigmentation, increased sweating, photosensitivity; seborrhoeic dermatitis, skin lesion, skin disorder, acne, hyperkeratosis, alopecia, urticaria, eczema, pruritus, skin discolouration, drug eruption, dandruff	*Less frequent*
Musculoskeletal and connective tissue disorders	muscle spasms, musculoskeletal pain, back pain, arthralgia, pain in the extremity	*Frequent*
	blood creatine phosphokinase increased, posture abnormal, joint stiffness, joint swelling, muscular weakness, neck pain, rhabdomyolysis	*Less frequent*
Renal and urinary disorders	Micturition disturbances or polyuria, enuresis, urinary incontinence	*Frequent*:
	Dysuria, pollakiuria, either due to polydipsia or hyponatraemia, urinary retention	*Less frequent*
Pregnancy, puerperium, and neonatal conditions	neonatal medicine withdrawal syndrome	*Less frequent*
Reproductive system and breast disorders	Amenorrhea; galactorrhoea; priapism; gynaecomastia, breast pain, breast discomfort, sexual and erectile dysfunction, menstrual disorder [(1)], dysmenorrhoea or menorrhagia, vaginal discharge, ejaculation disorder, menstruation delayed, breast engorgement, breast enlargement, breast discharge	*Less frequent*
General disorders and administration site conditions	Oedema [(1)], pyrexia, chest pain, asthenia, fatigue, pain	*Frequent*
	Face oedema, gait disturbance, gait abnormal, feeling abnormal, sluggishness, influenza like illness, thirst, chest discomfort, chills, body temperature increased, malaise, feeling abnormal, discomfort, medicine withdrawal syndrome,	*Less frequent*

	peripheral coldness, hypothermia, body temperature decreased, induration	
Injury, poisoning and procedural complications	fall	*Frequent*
	procedural pain	*Less frequent*

(1) Extrapyramidal disorder:

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 is 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 as in PMI RISPERIDONE 1 mg/ml.

Cardiac disorders

Postural orthostatic tachycardia syndrome.

Class effects

Cases of QT-prolongation have been reported post-marketing with risperidone. Other class-related cardiac effects reported with antipsychotics which prolong QT-interval include ventricular dysrhythmia, 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 medicines (frequency unknown).

Weight gain

The proportions of risperidone 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 (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 (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 to 12 years of age is 3 to 5 kg per year. From 12 to 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

ADRs 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 elderly patients with dementia. In addition, the following ADRs were reported with a frequency ≥ 5 % in elderly patients 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, the 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”).

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 SAHPRA website.

4.9 Overdose

Symptoms

Reported signs and symptoms have been those resulting from an exaggeration of the medicine's known pharmacological effects. Symptoms of acute overdosage include drowsiness, extrapyramidal symptoms, sedation, hypotension, seizures, convulsions and tachycardia. Electrocardiogram abnormalities, especially QT-prolongation have been reported. Torsades de pointes has been reported in association with combined overdose of oral risperidone as in PMI RISPERIDONE 1 mg/ml and paroxetine. In the case of acute overdosage, the possibility of multiple medicine involvement should be considered.

Treatment:

Establish and maintain a clear airway and ensure adequate oxygenation and ventilation.

Activated charcoal may be administered with a laxative.

Cardiovascular monitoring should be initiated immediately and should include continuous electrocardiographic monitoring to detect dysrrhythmias.

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. For treatment of severe extrapyramidal symptoms an anticholinergic medication should be administered. Close medical supervision and monitoring should continue until the patient recovers.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.6.5 Central nervous system depressants. Miscellaneous structures.

Pharmacotherapeutic group: Other antipsychotics, ATC Code: N05AX08

Risperidone is a benzisoxazole antipsychotic with a strong affinity for serotonin type 2 (5-HT_2) receptors and a slightly weaker affinity for dopamine type 2 (D2) receptors. Risperidone also has moderate affinity for the $alpha_1$-adrenergic, $alpha_2$-adrenergic, and H_1-histaminergic receptors. The affinity of risperidone for the serotonin 5-HT_{1A}, 5-HT_{1C} and 5-HT_{1D} receptors are low to moderate while its affinity for dopamine D_1 receptors and the haloperidol-sensitive sigma site is weak. Risperidone has negligible affinity for cholinergic-muscarinic, beta-adrenergic, and serotonin 5-HT_{1B} and 5-HT_3 receptors. It is a dopamine D2-antagonist.

5.2 Pharmacokinetic properties

Absorption

Risperidone is rapidly and extensively absorbed after oral administration, peak plasma concentrations being reached within 1 to 2 hours. Food does not significantly affect the extent of absorption of risperidone.

Distribution

Distribution is rapid and extensive.

Biotransformation:

Risperidone is extensively metabolised in the liver by hydroxylation to its main active metabolite, 9-hydroxyrisperidone, which has a similar pharmacological activity to risperidone. Risperidone and 9-hydroxy-risperidone form the active antipsychotic fraction. Hydroxylation is mediated by the cytochrome P-450 isoenzyme CYP2D6.

After oral administration to psychotic patients, risperidone's half-life is about 3 hours. The elimination half-life of 9-hydroxyrisperidone and the active psychotic fraction is 24 hours.

Steady state is reached within 1 day for risperidone in most patients and 4 - 5 days for 9-hydroxyrisperidone. Risperidone plasma concentrations is dose proportional within the therapeutic dose range. Risperidone is bound to albumin and alpha, - acid glycoprotein. Plasma protein binding of risperidone is 88 % and 77 % for 9-hydroxyrisperidone. One week after administration 70 % of the dose is excreted in the urine and 14 % in the faeces. In the urine risperidone and 9-hydroxyrisperidone represent 35 – 45 % of the dose. Risperidone showed significantly higher active plasma concentrations and slower elimination in the elderly and in patients with moderately severe 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 mild to moderate liver insufficiency.

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzoic acid

Tartaric Acid

Hydrochloric Acid

Purified Water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

An in use shelf-life of 100 days is approved for this product stored at or below 25 ^{0}C

6.4 Special precautions for storage

Store at or below 25 ºC or below. Do not freeze.

6.5 Nature and contents of container

30 ml; 60 ml, 100 ml or 120 ml Amber glass bottle (USP Type III) with white Light Density Polyethylene/Polypropylene child resistant, tamper evident cap. Additionally, a 4 ml dosing pipette is supplied in each pack consisting of a polystyrene plunger, Light Density Polyethylene barrel and piston, Light Density Polyethylene protective sheath (dosing pipette holder) and Polyethylene wiper. The dosing pipette is CE "Conformite Europeene" marked. The bottle and dosing pipette are packed in an outer cardboard container.

6.6 Special precautions for disposal and other handling

DIRECTIONS FOR OPENING THE BOTTLE AND USING THE PIPETTE

1. Push the plastic screw cap down while turning it counter clockwise. Remove the unscrewed cap.
2. Insert the pipette into the bottle. While holding down the barrel, pull the plunger up to the level that corresponds with the dosage required for administration.
3. While holding the plunger, remove the pipette from the bottle.
4. Empty the pipette into any non-alcoholic drink, except for tea, by sliding the plunger down.
5. Close the bottle and rinse the pipette.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unimed Healthcare (Pty) Ltd

Corner Birch Road & Bluegum Avenue,

Anchorville,

Lenasia, 1827

South Africa

Tel: + 2711 056 6999

8. REGISTRATION NUMBER

43/2.6.5/0691

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Date of registration: 11 June 2018

10. DATE OF REVISION OF THE TEXT

To be allocated

PATIENT INFORMATION LEAFLET

Scheduling Status: S5

PMI RISPERIDONE 1 mg/ml (Oral solution):

Risperidone

Sugar free

Preservative: Benzoic Acid 0,15 % *m/v*

Please read this leaflet carefully before you start taking PMI RISPERIDONE 1 mg/ml

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet:

1. What PMI RISPERIDONE 1 mg/ml contains

PMI RISPERIDONE 1 mg/ml contains active ingredient risperidone, which belongs to the class of medicine called atypical antipsychotics.

PMI RISPERIDONE 1 mg/ml is indicated for:

- Schizophrenia, where you may hear voices, see things, or sense things that are not there, believe things that are not true or feel unusually suspicious or confused.
- Behavioural disturbances in patients with dementia who may have symptoms such as aggressiveness, verbal outbursts, physical violence, agitation and slow or pointless movement.
- 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 judgement, including disruptive or aggressive behaviour.
- Children (aged 5 – 12 years) with lower-than-average intellectual functioning or mental retardation that show antisocial and destructive behaviour, including violence towards people and animals, destruction of property, lying, stealing, running away from home, being impulsive and wanting to cause injury to themselves.

2. What you need to know before you take PMI RISPERIDONE 1 mg/ml

Do not take PMI RISPERIDONE 1 mg/ml:

- If you are hypersensitive (allergic) to risperidone or any of the other ingredients of PMI RISPERIDONE 1 mg/ml (listed in section 6).
- Do not give this medicine to children under 5 years with conduct and other disruptive behaviour disorders.
- If you suffer from a type of dementia called Lewy body dementia and Parkinson’s disease.

Warnings and precautions

Tell your doctor or health care provider before you take PMI RISPERIDONE 1 mg/ml oral solution:

- If you suffer from kidney or liver function impairment.
- If you experience any signs of possible Tardive dyskinesia (TD) such as sudden uncontrollable movements of voluntary muscle groups. Signs can consist of coordinated, constant movements of the mouth, tongue, jaw and cheeks and in some cases movement in your arms and legs. The risk of developing TD and the chance that it will become permanent is thought to increase with the length of therapy and the overall dose taken by the patient. This condition can develop after a brief period of therapy at low doses, although this is much less common. There is known treatment for TD, but it may go away partially or completely if therapy is stopped.
- If you experience any signs of Neuroleptic Malignant Syndrome (NMS) which is a potentially serious side effect reported with PMI RISPERIDONE 1 mg/ml which may cause death. Signs may include that your muscles are constantly tense, your body temperature is very high, shaking, confusion, sweating, your heart beats very rapidly or blood pressure or muscle pain and weakness. Treatment with PMI RISPERIDONE 1 mg/ml should be stopped immediately if you have NMS.
- If you know of any factors which would favour you having a stroke, such as high blood pressure, cardiovascular disorder, current smoking or blood vessel problems in the brain or if you are older than 80 years
- If you experience signs of cerebrovascular adverse events, such as a stroke. Signs may include that you cannot move or feel one side of your body, you may be confused and have difficulty to say words and follow commands.

- If you suffer from epilepsy (a condition causing seizures). PMI RISPERIDONE 1 mg/ml may worsen the symptoms of this condition.
- If you have a heart problem. Examples include an irregular heart rhythm, or if you are prone to low blood pressure. PMI RISPERIDONE 1 mg/ml may cause low blood pressure due to its alpha blocking activity. Your dose needs to be adjusted.
- If you are using a water tablet (diuretic) called furosemide. Studies have shown that older adults with dementia who are treated with furosemide and PMI RISPERIDONE 1 mg/ml are at an increased risk of death when compared to patients being treated with only PMI RISPERIDONE 1 mg/ml. Drink plenty of fluids, especially in hot weather and avoid becoming dehydrated while you are taking this medication.
- If you have an abnormally high level of the hormone prolactin in your blood or if you have a tumour, which is possibly dependant on prolactin. PMI RISPERIDONE 1 mg/ml commonly raises levels of prolactin. This may cause side effects such as menstrual disorders or fertility problems in women, breast swelling in men (see section 4). If such side effects occur, evaluation of the prolactin level in blood is recommended.
- If you have or think you might have diabetes. As diabetes mellitus or worsening of pre-existing diabetes mellitus has been seen in patients taking PMI RISPERIDONE 1 mg/ml, your doctor should check for signs of high blood sugar. In patients with pre-existing diabetes mellitus, blood glucose should be monitored regularly.
- If you have abnormally high levels of blood sugar. Signs may include frequently feeling very hungry and or thirsty, urinating frequently, blurred vision, sleepiness and dry mouth.
- If you have problems maintaining your weight. This medicine may cause you to gain weight. Significant weight gain can adversely affect your health. Your doctor should regularly measure your body weight. Avoid overeating.
- If you are a man and you have ever had prolonged or painful erection.

- If you have problems controlling your body temperature or overheating.
- If you or someone else in your family has a history of blood clots, as antipsychotics have been associated with formation of blood clots.
- If you are planning to have an operation on your eye, make sure you tell your doctor that you are taking PMI RISPERIDONE 1 mg/ml. During an operation on the eye for cloudiness of the lens (cataract), the pupil (the black circle in the middle of your eye) may not increase in size as needed. Also, the iris (the coloured part of the eye) may become floppy during surgery and that may lead to eye damage.
- If you know that you have had low levels of white blood cells in the past (which may or may not have been caused by other medicines). Your doctor may check your white blood cell counts.
- If you have a brain tumor, intestinal obstruction or Reye's syndrome (a serious condition that causes swelling in the liver and brain).

Elderly people with dementia

In elderly patients with dementia, there is an increased risk of stroke. You should not take PMI RISPERIDONE 1 mg/ml if you have dementia caused by stroke.

Medical treatment should be sought straight away if you or your caregiver notice a sudden change in your mental state or sudden weakness or numbness of your face, arms or legs, especially on one side, or slurred speech, even for a short period of time. These may be signs of a stroke.

During treatment with PMI RISPERIDONE 1 mg/ml you should frequently see your doctor.

Children and adolescents

PMI RISPERIDONE 1 mg/ml should be used with caution in young children and adolescents with conduct disorder. Before treatment is started for conduct disorder, other causes of aggressive

behaviour should have been ruled out. If PMI RISPERIDONE 1 mg/ml has been prescribed for your child, inform your doctor if you notice that your child is tired or sleepy as this may impact learning ability.

A change in the time of administration might improve attention difficulties.

Before treatment is started your child's body weight may be measured, and it may be regularly monitored during treatment.

Using other medicines with PMI RISPERIDONE 1 mg/ml

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Tell your doctor or pharmacist if you are taking any other medicines, including any you have bought at your pharmacy, supermarket or health food shop. Please consult your doctor, pharmacist or other healthcare professional for advice.

The following medicine may reduce the effect of PMI RISPERIDONE 1 mg/ml

- Carbamazepine, phenytoin, phenobarbital (medicines for treating epilepsy)
- Clozapine (medicine for treating schizophrenia)
- Rifampicin (a medicine for treating some infections)

The following medicine may increase the effect of PMI RISPERIDONE 1 mg/ml

- Antidepressants such as fluoxetine and paroxetine as well as venlafaxine and tricyclic antidepressants
- Cimetidine and ranitidine (medicine for treating heartburn or stomach ulcers)
- Medicines known as beta-blockers (for the treatment of high blood pressure)
- Phenothiazines (e.g. used to treat psychosis or to calm down)
- Quinidine (used for certain types of heart disease)
- Itraconazole and ketoconazole (medicines for treating fungal infections)

- Certain medicines used in the treatment of HIV/AIDS, such as ritonavir
- Verapamil, a medicine used to treat high blood pressure and/or abnormal heart rhythm
- Sertraline and fluvoxamine, medicines used to treat depression and other psychiatric disorders.

It is very important to tell your doctor, pharmacist or healthcare provider if you take any of the following:

- Water tablets (diuretics) used to treat certain heart problems or swelling of body parts due to build up of too much fluid such as furosemide (refer to "Warnings and precautions")
- Alcohol or medicines that work on your brain such as medicines to calm you down (benzodiazepines), some medicines for pain (opiates), medicines for allergies (certain antihistamines) as PMI RISPERIDONE 1 mg/ml may increase the sedative effect of them all.
- Medicines that may change the electrical activity of your heart, such as medicines for malaria (such as quinidine and mefloquine), heart rhythm problems (such as amiodarone, quinidine), allergies (antihistamines), some antidepressants (such as amitriptyline, maprotiline) or other medicines for mental problems
- Medicines that cause a slow heartbeat
- Medicines that cause low blood potassium (such as certain diuretics)
- Medicines that increase the activity of the central nervous system (psychostimulants, such as methylphenidate)
- Lithium (used to treat certain types of depression)
- Medicines to treat Parkinson's disease such as levodopa
- Valproate (used to treat epilepsy and seizures)

- Topiramate (medicine used to treat epilepsy) does not have a significant effect on the level of PMI RISPERIDONE 1 mg/ml in the blood.
- Medicines to lower your blood pressure
- Paliperidone (a medicine used to treat mental disorders including schizophrenia)
- Erythromycin (an antibiotic) does not have an effect on level of PMI RISPERIDONE 1 mg/ml in the blood.
- Galantamine and donezepil (medicines used to treat dementia) do not have an effect on PMI RISPERIDONE 1 mg/ml.

PMI RISPERIDONE 1 mg/ml with food and drink and alcohol

Taking alcohol during treatment with PMI RISPERIDONE 1 mg/ml may have additive CNS depressant effects. PMI RISPERIDONE 1 mg/ml can be taken with or without food.

Pregnancy and breastfeeding and fertility

The safety of PMI RISPERIDONE 1 mg/ml in pregnant and breast-feeding women has not yet been established.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist, or other health care provider for advice before taking PMI RISPERIDONE 1 mg/ml.

Shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems and difficulty in feeding, have been observed in newborns, if a mother used PMI RISPERIDONE 1 mg/ml in the last trimester of her pregnancy.

Driving and using machinery

PMI RISPERIDONE 1 mg/ml may cause sleepiness and a lack of concentration. It is not always possible to predict to what extent PMI RISPERIDONE 1 mg/ml may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which PMI RISPERIDONE 1 mg/ml affects them.

PMI RISPERIDONE 1 mg/ml contains benzoic acid

PMI RISPERIDONE 1 mg/ml contains 1,50 mg of benzoic acid in each ml of oral solution. Benzoic acid may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

3. How to take PMI RISPERIDONE 1 mg/ml

Do not share medicines prescribed for you with any other person.
Always take PMI RISPERIDONE 1 mg/ml exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. If you have the impression that the effect of PMI RISPERIDONE 1 mg/ml is too strong or too weak, talk to your doctor or pharmacist.

Treatment of schizophrenia

If you are already using an antipsychotic medicine, your doctor may gradually discontinue this treatment when switching to PMI RISPERIDONE 1 mg/ml. If you are receiving a depot injection, your doctor will initiate PMI RISPERIDONE 1 mg/ml treatment in place of the next scheduled injection.

You may take PMI RISPERIDONE 1 mg/ml either once daily or twice daily.

Initial adult dose: The usual dose is 2mg per day. Your doctor may increase the dosage to 4mg per day on the second day.

Maintenance dose: Your doctor will decide what the optimum maintenance dose is based on your response.

Liver and kidney impairment:

Your doctor should halve both the starting dose and the subsequent dosage increases if you suffer for liver or kidney impairment.

Elderly patients:

The starting dose is usually 0,5 mg twice daily. Your doctor may increase the dose up to 1 – 2 mg twice daily.

Children:

PMI RISPERIDONE 1 mg/ml should not be used in children under the age of 15 years.

Treatment of mania in bipolar disorders

The starting dose will normally be 2 mg once a day and your dose may gradually be adjusted by your doctor depending on how you respond to the treatment. Efficacy was demonstrated in flexible doses over a range of 1 mg to 6 mg per day.

Treatment of behavioural disturbances in patients with dementia

The usual starting dose is 0,25 mg twice daily. Your doctor may increase the dose to a maintenance dose of 0,5 mg to 1 mg twice daily.

Treatment of conduct and other disruptive behaviour disorders in children 5 – 12 years of age

A doctor only will decide this treatment and dosage. The usual starting dose is 0,01 mg per kg once daily. The doctor may increase the dose to a maintenance dose of 0,02 – 0,04 mg per kg once daily.

Children under 5 years old should not be treated with PMI RISPERIDONE 1 mg/ml for conduct and disruptive behaviour disorders.

DIRECTIONS FOR OPENING THE BOTTLE AND USING THE PIPETTE

1. Push the plastic screw cap down while turning it counter clockwise. Remove the unscrewed cap.
2. Insert the pipette into the bottle. While holding down the barrel, pull the plunger up to the level that corresponds with the dosage required for administration.
3. While holding the plunger, remove the pipette from the bottle.
4. Empty the pipette into any non-alcoholic drink, except for tea, by sliding the plunger down.
5. Close the bottle and rinse the pipette.

If you take more PMI RISPERIDONE 1 mg/ml than you should

In the event of overdose, one or more of the following symptoms may occur: reduced consciousness, drowsiness, sleepiness, excessive trembling, excessive muscle stiffness, fast beating heart and low blood pressure. Cases of abnormal electrical conduction in the heart (QT prolongation) and convulsion have been reported. Overdose can happen if you are taking other medications together with PMI RISPERIDONE 1 mg/ml.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre. Take the remaining solution and/or the container with you to the hospital so that the doctor knows what you have taken. There is no specific antidote for risperidone overdose.

If you forget to take PMI RISPERIDONE 1 mg/ml

If you missed a dose, take it as soon as you remember. If it is almost time for you next dose, skip the missed dose and continue to take the solution at the usual time. Do not take a double or larger dose to make up for the forgotten individual doses.

If you have trouble remembering when to use your medicine, ask your pharmacist for some hints.

If you stop taking PMI RISPERIDONE 1 mg/ml

You should not stop taking PMI RISPERIDONE 1 mg/ml unless told to do so by your doctor. Your symptoms may return. If your doctor decides to stop PMI RISPERIDONE 1 mg/ml, your dose may be decreased gradually over a few days.

4. Possible side effects

PMI RISPERIDONE 1 mg/ml can cause side effects. Not all side effects reported for PMI RISPERIDONE 1 mg/ml are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking PMI RISPERIDONE 1 mg/ml, please consult your health care provider for advice.

If any of the following happen, stop taking PMI RISPERIDONE 1 mg/ml and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Fast or irregular heart beat

- Difficult or unusually fast breathing, high fever, irregular blood pressure, loss of bladder control, severe muscle stiffness, seizures, unusual pale skin, tiredness or weakness, could be signs of Neuroleptic Malignant Syndrome.
- Cough difficulty swallowing, dizziness, hives, itching, tightness in chest, wheezing and puffiness or swelling of eyelids, face, lips or tongue.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to PMI RISPERIDONE 1 mg/ml. You may need urgent medical attention or hospitalization.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- chest pain;
- angina;
- experience blood clots in the veins, especially in the legs (symptoms include swelling, pain, and redness in the leg), which may travel through blood vessels to the lungs causing chest pain and difficulty breathing. If you notice any of these symptoms seek medical advice immediately;
- have dementia and experience a sudden change in your mental state or sudden weakness or numbness of your face, arms, or legs, especially on one side, or slurred speech, even for a short period of time. These may be signs of a sudden loss of blood supply to the brain (stroke or “mini” stroke);
- are a man and experience prolonged or painful erection. This is called “priapism”. Immediate medical treatment may be needed
- Tardive dyskinesia (twitching or jerking movements that you cannot control in your face, tongue, or other parts of your body). Tell your doctor immediately if you experience

involuntary rhythmic movements of the tongue, mouth and face. Withdrawal of PMI RISPERIDONE 1 mg/ml may be needed;

- signs of recurrent infections such as fever or sore throat;
- fever, chills, weakness, sore throat, sores in the mouth or throat, bleeding gums, bone pain, low blood pressure, fast heartbeat, and trouble breathing, signs of agranulocytosis
- less urine than is normal for you;
- yellowing of the skin and eyes, dark urine, and tiredness which may be symptoms of liver problems.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- Pneumonia, infection of the chest (bronchitis), common cold symptoms, sinus infection, urinary tract infection, ear infection, feeling like you have the flu;
- Anxiety;
- Muscle spasm of face, neck and back, twitching movements, weakness of arms or legs (Parkinsonism);
- Difficulty in speaking or swallowing, loss of balance control, trembling and shaking of hands and fingers; tremor
- Insomnia (sleeplessness); weakness; fatigue; lassitude; drowsiness; headache; increased dream activity; increased duration of sleep;
- Changes in vision and blurred vision, inflammation of the eye “pink eye”;
- Rapid heart rate and high blood pressure;
- Shortness of breath, cough, sore throat, nose bleeds, stuffy nose, pain in the throat;

- Constipation, diarrhoea; dyspepsia; vomiting; nausea, abdominal pain, dry mouth, stomach discomfort, toothache;
- Skin rash or itching, redness;
- Problems in urination or increase in amount of urine;
- Weight gain, increased appetite or decreased appetite;
- Mood or mental changes, including aggressive behaviour, agitation, difficulty in concentration and memory problems.
- Unusual secretion of milk; sexual dysfunction or decrease libido; menstrual changes.
- Back pain, joint pain, muscle spasms, pain in the muscles and bones, pain in extremity;
- falls
- Swelling of the body, arms or legs, fever, chest discomfort, weakness, fatigue (tiredness), pain;
- PMI RISPERIDONE 1 mg/ml can raise your levels of a hormone called "prolactin" found on a blood test (which may or may not cause symptoms). When symptoms of high prolactin occur, they may include in men breast swelling, difficulty in getting or maintaining erections, or other sexual dysfunction. In women they may include breast discomfort, leakage of milk from the breasts, missed menstrual periods, or other problems with your cycle.

Less frequent side effects:

- Infection of the breathing passages, bladder infection, eye infection, tonsillitis, fungal infection of the nails, infection of the skin, an infection confined to a single area of skin or part of the body, viral infection, skin inflammation caused by mites; ear infection and chronic ear infection;

- Decrease in the type of white blood cells that help to protect you against infection, white blood cell counts decreased, decrease in platelets (blood cells that help you stop bleeding), anaemia, decrease in red blood cells, increase in eosinophils (a type of white blood cell) in your blood;
- Confusion, decreased sexual drive, listless, nervousness, delayed orgasm, elated mood (mania) or depressed mood (hypomania), nightmares, sleep walking, sleep related eating disorder;
- Unresponsive to stimuli, loss of consciousness, low level of consciousness;
- Convulsion (fits), fainting;
- A restless urge to move parts of your body, balance disorder, abnormal coordination, dizziness upon standing, disturbance in attention, problems with speech, loss or abnormal sense of taste, reduced sensation of skin to pain and touch, a sensation of tingling, pricking, or numbness of skin;
- Oversensitivity of the eyes to light, dry eye, increased tears, redness of the eyes;
- Glaucoma (increased pressure within the eyeball), eye rolling, eye movement disorder, eyelid margin crusting;
- Eye problem during cataract surgery. During cataract surgery, a condition called intraoperative floppy iris syndrome (IFIS) can happen if you take or have taken PMI RISPERIDONE 1 mg/ml. If you need to have cataract surgery, be sure to tell your doctor if you take or have taken PMI RISPERIDONE 1 mg/ml.
- Sensation of spinning (vertigo), ringing in the ears, ear pain;
- Atrial fibrillation (an abnormal heart rhythm), an interruption in conduction between the upper and lower parts of the heart, abnormal electrical conduction of the heart, prolongation of the QT interval from your heart, slow heart rate, abnormal electrical tracing of the heart (electrocardiogram or ECG), a fluttering or pounding feeling in your chest (palpitations);

- Low blood pressure, low blood pressure upon standing (consequently, some people taking PMI RISPERIDONE 1 mg/ml may feel faint, dizzy, or may pass out when they stand or sit up suddenly, flushing;
- Pneumonia caused by inhaling food, lung congestion, congestion of breathing passages, crackly lung sounds, wheezing, voice disorder, breathing passage disorder;
- Trouble breathing during sleep (apnoea), fast, shallow breathing;
- Stomach or intestinal infection, stool incontinence, very hard stool, difficulty swallowing, excessive passing of gas or wind;
- Inflammation of the pancreas, a blockage in the bowels, swollen tongue, chapped lips; gastroenteritis “stomach bug”, decreased contraction of the intestines (ileus)
- Hives (or "nettle rash"), itching, hair loss, thickening of skin, eczema, dry skin, skin discolouration, acne, dandruff, skin disorder, skin lesion, increased sweating, skin discoloration, rash on skin related to a drug, dandruff;
- Frequent passing of urine, inability to pass urine, pain when passing urine;
- Symptoms of medicine withdrawal including in newborns
- Erectile dysfunction, ejaculation disorder;
- Loss of menstrual periods, missed menstrual periods or other problems with your cycle (females);
- Development of breasts in men, leakage of milk from the breasts, sexual dysfunction, breast discomfort, vaginal discharge, breast enlargement, breast discharge;
- Inappropriate secretion of a hormone that controls urine volume;
- Diabetes or worsening of diabetes, high blood sugar, excessive drinking of water
- Dangerously excessive intake of water, increased insulin (a hormone that controls blood sugar levels) in your blood, life threatening complications of uncontrolled diabetes, coma due to uncontrolled diabetes;

- Sugar in the urine, low blood sugar, high blood triglycerides (fats);
- Muscle weakness, muscle pain, neck pain, joint swelling, joint stiffness, abnormal posture increased blood creatinine phosphokinase (seen on a blood test) breakdown of muscle fibres and pain in muscles (rhabdomyolysis);
- Increased liver transaminases in your blood, increased GGT (a liver enzyme called gamma-glutamyltransferase) in your blood, increased liver enzymes in your blood;
- Swelling of the face, sluggishness, chills, an increase in body temperature, a change in the way you walk, feeling thirsty, feeling unwell, feeling out of sorts, discomfort, hardening of skin;
- Decreased body temperature, coldness in arms and legs;
- Procedural pain.

Frequency unknown side effect

- Reduced visual acuity.

The following side effect has been seen with the use of another medicine called paliperidone that is very similar to risperidone (as in RISPIDE), so these can also be expected with RISPIDE: rapid heartbeat upon standing.

The following side effects were reported more often in children and adolescents (5 to 17 years) than in adults: feeling sleepy or less alert, fatigue (tiredness), headache, increased appetite, vomiting, common cold symptoms, nasal congestion, abdominal pain, dizziness, cough, fever, tremor (shaking), diarrhoea, and incontinence (lack of control) of urine.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of PMI RISPERIDONE 1 mg/ml.

5. How to store PMI RISPERIDONE 1 mg/ml

- Store at or below 25 °C or below. Do not freeze. Keep well closed.
- Once opened the product can be stored at or below 25 ºC for 100 days.
- KEEP ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN
- Do not use the solution after the expiry date printed on the label/container.
- Return all unused medicine to your pharmacist
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets)

6. Contents of the pack and other information

What PMI RISPERIDONE 1 mg/ml contains

PMI RISPERIDONE 1 mg/ml contains the active ingredient risperidone. Each 1 ml of oral solution contains 1 mg of risperidone.

Inactive ingredients: Benzoic acid (preservative 0,15 % m/v), hydrochloric acid, tartaric acid and purified water.

What PMI RISPERIDONE 1 mg/ml looks like and contents of the pack

Clear colourless solution free from foreign particles.

30 ml; 60 ml, 100 ml or 120 ml Amber glass bottle (USP Type III) with white Light Density Polyethylene/Polypropylene child resistant, tamper evident cap. Additionally a 4 ml dosing pipette

is supplied in each pack consisting of a polystyrene plunger, Light Density Polyethylene barrel and piston, Light Density Polyethylene protective sheath (dosing pipette holder) and Polyethylene wiper. The dosing pipette is CE "Conformite Europeene" marked. The bottle and dosing pipette are packed in an outer cardboard container

Holder of Certificate of Registration

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This leaflet was last revised in

To be allocated

Registration number

43/2.6.5/0691