

Professional Information for Medicines for Human Use

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE
PRAMISUL 50 mg (tablets)
PRAMISUL 200 mg (tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PRAMISUL 50 mg:
Each tablet contains 50 mg of amisulpride.
Excipients with known effect: lactose monohydrate 50,00 mg

PRAMISUL 200 mg:
Each tablet contains 200 mg of amisulpride.
Excipients with known effect: lactose monohydrate 200,00 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

PRAMISUL 50 mg:
White to off-white, round shaped uncoated tablets with break line on one side and marking "L 73" on other side.

PRAMISUL 200 mg:
White to off-white, round shaped uncoated tablets with break line on one side and marking "L 75" on other side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications
PRAMISUL is indicated for the treatment of patients with acute and chronic schizophrenia, including patients characterized by predominant negative symptoms.

4.2. Posology and method of administration

Posology
No specific titration is required when initiating the treatment with **PRAMISUL** and doses should be adjusted according to the individual response.

PRAMISUL can be administered once daily at oral doses up to 400 mg, higher doses should be administered twice daily.

For acute schizophrenia:
Oral doses between 400 - 800 mg/day are recommended. In individual cases, the dose may be increased up to 1 200 mg/day. Doses above 1 200 mg/day have not been evaluated for safety and therefore should not be used.

For patients with mixed positive and negative symptoms:

Doses should be adjusted to obtain optimal control of positive symptoms. Maintenance treatment should be established individually with the minimum effective dose.

For patients characterised by predominant negative symptoms:

Doses between 50 – 100 mg/day are recommended.

Doses should be adjusted individually.

Elderly:
Particular caution should be used due to a possible risk of hypotension or sedation.

Hepatic insufficiency:
Since **PRAMISUL** is weakly metabolised, a dosage reduction should not be necessary.

Renal impairment:
PRAMISUL is eliminated by renal route. In renal insufficiency, the dose should be reduced to half in patients with creatinine clearance (CrCl) between 30 - 60 mL/min and to a third in patients with CrCl between 10 - 30 mL/min (see section 4.4).

As there is no experience in patients with severe renal impairment (CrCl < 10 mL/min), these patients should not receive **PRAMISUL.**

Method of administration

For oral use.

4.3. Contraindications

PRAMISUL is contraindicated in:
- Hypersensitivity to amisulpride or to any of the constituents of **PRAMISUL** listed in section 6.1.
- Concomitant use of other medicines that could induce or enhance the risk of torsades de pointes and/or prolong the QT - interval (see section 4.4 and 4.5).
- Congenital QT - interval prolongation
- Concomitant prolactin-dependent tumours e.g. pituitary gland prolactinomas and breast cancer.
- Phaeochromocytoma
- Pregnancy and lactation (see section 4.6)
- Children under 15 years of age.
- Women of childbearing potential unless using adequate contraception.
- Severe renal function impairment (see section 4.2)
- Combination with the following medicines which could induce Torsades de Pointes:
  Class IA antidysrhythmic medicines such as quinidine disopyramide
  Class III antidysrhythmic medicines such as amiodarone, sotalol
- Other medicines such as bepridil, cisapride, sultopride, thioridazine, methadone, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin (see section 4.5).
- Combination with levodopa (see section 4.5).

4.4. Special warnings and precautions for use

Neuroleptic Malignant Syndrome
Neuroleptic Malignant Syndrome, a potentially fatal complication, characterized by hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated Creatinine Phosphokinase (CPK), may occur. In the event of hyperthermia, particularly with high daily doses, all antipsychotic medicine including **PRAMISUL** should be discontinued.

Hyperglycaemia
Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported with some atypical antipsychotic agents. Patients with an established diagnosis of diabetes mellitus, who are started on **PRAMISUL ,** 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 **PRAMISUL** should be monitored for symptoms of hyperglycaemia including polydipsia, polyuria, polyphagia and weakness. Patients who develop symptoms of hyperglycaemia during treatment with **PRAMISUL** should undergo fasting blood glucose testing. In some cases, hyperglycaemia may resolve when **PRAMISUL** is discontinued. However, some patients could require continuation of anti-diabetic treatment despite discontinuation of the suspect medicine.

Renal Insufficiency
PRAMISUL is eliminated by the renal route. In cases of renal insufficiency, the dose should be decreased or intermittent treatment could be considered (see section 4.2).

Seizure

PRAMISUL may lower the seizure threshold. Therefore, patients with a history of epilepsy should be closely monitored during therapy with **PRAMISUL.**

Elderly
In elderly patients, **PRAMISUL**, should be used with particular caution because of a possible risk of hypotension or sedation. Reduction in dosage may also be required because of renal insufficiency.

Parkinson's disease
Caution should be exercised when prescribing **PRAMISUL** to patients with Parkinson's disease since it may cause worsening of the disease. **PRAMISUL** should be used only if neuroleptic treatment cannot be avoided.

Acute withdrawal symptoms
Acute withdrawal symptoms including nausea, vomiting and insomnia have been described after abrupt cessation of high doses of antipsychotic medicine. Recurrence of psychotic symptoms may also occur, and the emergence of involuntary movement disorders (such as akathisia, dystonia and dyskinesia) has been reported with **PRAMISUL** (see section 4.8). Therefore, gradual withdrawal of **PRAMISUL** is advisable.

Prolongation of the QT interval
Caution should be exercised when **PRAMISUL** is prescribed in patients with known cardiovascular disease or family history of QT prolongation. **PRAMISUL** induces a dose-dependent prolongation of the QT interval (see section 4.8). This effect is known to potentiate the risk of serious ventricular dysrhythmias such as Torsade de Pointes. Before any administration, and if possible according to the patient's clinical status, it is recommended to exclude the following factors which could favour the occurrence of this rhythm disorder:

- bradycardia less than 55 bpm
- cardiac disease or family history of sudden death or QT prolongation
- electrolyte imbalance, in particular hypokalaemia
- congenital prolongation of the QT interval
- on-going treatment with a medicine likely to produce pronounced bradycardia (< 55 bpm), hypokalaemia, decreased intracardiac conduction, or prolongation of the QT interval (see section 4.5).

Baseline ECG is recommended prior to treatment in all patients especially in the elderly and patients with a positive personal or family history of cardiac disease or abnormal findings on cardiac clinical examination. During therapy, the need for ECG monitoring (e.g. at dose escalation) should be assessed on an individual patient basis. The dose of **PRAMISUL** should be reduced if QT is prolonged and discontinued if QTc is > 500 ms.

Periodic electrolyte monitoring is recommended particularly if the patient is taking diuretics or during inter-current illness.

Concomitant use with antipsychotics should be avoided (see section 4.5).

Stroke:
In randomized clinical trials versus placebo performed in a population of elderly patients with dementia and treated with certain atypical antipsychotic medicines, a 3-fold increase of the risk of cerebrovascular events has been observed. The mechanism of such risk increase is not known. An increase in the risk with other antipsychotic medicines, or other populations of patients cannot be excluded. **PRAMISUL** should be used with caution in patients with stroke risk factors.

Elderly patients with dementia:
Elderly patients with dementia-related psychosis treated with antipsychotic medicines are at an increased risk of death. Although the causes of death in clinical trials with atypical antipsychotics were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic medicines, treatment with conventional antipsychotic medicines may increase mortality.

PRAMISUL is not licensed for the treatment of dementia-related behavioural disturbances.

Venous thromboembolism (VTE)
Cases of VTE have been reported with antipsychotic medicinal products. 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 **PRAMISUL** and preventive measures undertaken.

Breast cancer:
PRAMISUL may increase prolactin levels. Therefore, caution should be exercised and patients with a history or a family history of breast cancer should be closely monitored during therapy with **PRAMISUL**.

Blood dyscrasias
Leukopenia, neutropenia and agranulocytosis have been reported with antipsychotics, including **PRAMISUL**. Unexplained infections or fever may be evidence of blood dyscrasias (see section 4.8), and requires immediate haematological investigation.

Lactose
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take **PRAMISUL.**

4.5. Interaction with other medicines and other forms of interaction

Contraindicated combinations
- Medicines which could induce Torsade de Pointes:
  - Class IA antidysrhythmics such as quinidine and disopyramide
  - Class III antidysrhythmics such as amiodarone and sotalol
  - Other medicines such as bepridil, cisapride, sultopride, thioridazine, methadone, erythromycin (intravenous application), vincamine (intravenous application), halofantrine, pentamidine, sparfloxacin, azole antifungals (see section 4.3).
- Levodopa: reciprocal antagonism of effects between levodopa and neuroleptics. **PRAMISUL** may oppose the effect of dopamine agonists e.g. bromocriptine, ropinirole.

Combinations not recommended
- Medicines which enhance the risk of torsade de pointes or could prolong the QT interval:
  - bradycardia-inducing medicines such as beta blockers, bradycardia-inducing calcium channel blockers such as diltiazem and verapamil, clonidine, guanfacine; and digitalis
  - medicines which induce hypokalaemia or electrolyte imbalance: hypokalaemic diuretics, stimulant laxatives, amphotericin B (intravenous application), glucocorticoids, and tetracosactides. Hypokalaemia should be corrected (see section 4.3)
  - antipsychotics such as pimozide, and haloperidol (see section 4.3)
  - imipramine antidepressants
  - lithium
  - some antihistamines such as astemizole, and terfenadine
  - mefloquine
- **PRAMISUL** may enhance the central effects of alcohol. Therefore alcohol should not be consumed during treatment.

Combinations which require precaution for use

Concomitant use of the following agents can lead to potentiation of the effect:
- CNS depressants including narcotics, anaesthetics, analgesics, sedative H1 antihistamines, barbiturates, benzodiazepines and other anxiolytic medicines, clonidine and derivatives
- Antihypertensive medicines and other hypotensive medicines.

4.6. Fertility, pregnancy and lactation
Safety of use of **PRAMISUL** during pregnancy and lactation has not been established.

Women of childbearing age
For women of childbearing potential, effective contraception should be fully discussed with the physician prior to treatment.

Pregnancy

Use of **PRAMISUL** is contraindicated during pregnancy (see section 4.3).

Neonates exposed to antipsychotics (including **PRAMISUL**) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery (see section 4.8). There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Lactation
It is not known whether **PRAMISUL** is excreted in breast milk, breastfeeding is therefore contraindicated (see section 4.3).

Fertility
In animal studies, a decrease in fertility linked to the pharmacological effects of the medicine (prolactin mediated effect) was observed.

4.7. Effects on ability to drive and use machines
When used as recommended, **PRAMISUL** may cause somnolence that can impair the ability to drive or operate heavy machinery.

4.8. Undesirable effects

a. ***Summary of the safety profile***
At the beginning of the treatment constipation, nausea, vomiting and dry mouth commonly occur.
Extrapyramidal symptoms also commonly occur: tremor, rigidity, hypokinesia, hypersalivation, akathisia and dyskinesia.

b. ***Tabulated list of adverse reactions***

System organ class	Frequent	Less frequent
Immune system disorders		Allergic reaction
Endocrine disorders	Galactorrhoea, amenorrhoea, or menstrual disorders, gynaecomastia, breast pain or enlargement, prolactinoma (see section 4.3), erectile dysfunction	
Metabolism and nutrition disorders		Hyperglycaemia (see section 4.4)
Psychiatric disorders	Insomnia, anxiety, agitation, orgasmic dysfunction	
Nervous system disorders	Extrapyramidal symptoms may occur: tremor, rigidity, hypokinesia, hypersalivation, akathisia, dyskinesia, acute dystonia (spasm torticollis, oculogyric crisis, trismus), somnolence	Tardive dyskinesia characterized by rhythmic, involuntary movements primarily of the tongue and/or face have been reported, usually after long term administration
Cardiac disorders	Hypotension	Bradycardia
Gastrointestinal disorders	Constipation, nausea, vomiting, dry mouth	
General disorders and administration site conditions:		Nausea, vomiting and insomnia, recurrence of psychotic symptoms, emergence of involuntary movement disorders (such as akathisia, dystonia and dyskinesia) (see section 4.4).
Investigations	Weight gain	Elevations of hepatic enzymes, mainly transaminases

Post Marketing data

	Frequency of occurrence
System Organ Class	**Frequency not known**
Blood and Lymphatic system disorders	Leukopenia, neutropenia, agranulocytosis (see section 4.4)
Metabolism and nutrition disorders	Hypertriglyceridemia, hypercholesterolemia
Psychiatric disorders	Confusion
Nervous system disorders	Neuroleptic Malignant Syndrome (see section 4.4), which is a potentially fatal complication
Cardiac disorders	QT interval prolongation and ventricular arrhythmias such as torsade de pointes, ventricular tachycardia, which may result in ventricular fibrillation or cardiac arrest, sudden death (see section 4.4).
Vascular disorders	Cases of venous thromboembolism, including cases of pulmonary embolism, sometimes fatal, and cases of deep vein thrombosis have been reported with antipsychotic medicines.
Skin and subcutaneous tissue disorders	Angioedema, urticaria
Pregnancy, puerperium and perinatal conditions	Medicine withdrawal syndrome in neonates (see section 4.6)

c. Description of selected adverse reactions

Increased Prolactin levels
Amisulpride causes an increase in plasma prolactin levels, which is reversible after medicine discontinuation. This may result in galactorrhoea, amenorrhoea, or menstrual disorders, gynaecomastia, breast pain or enlargement, prolactinoma (see section 4.3) and erectile dysfunction.

Extrapyramidal symptoms
Tremor, rigidity, hypokinesia, hypersalivation, akathisia, dyskinesia are generally mild at optimal dosages and partially reversible without discontinuation of **PRAMISUL** upon administration of antiparkinsonian medication. The incidence of extrapyramidal symptoms which is dose related, remains very low in the treatment of patients with predominantly negative symptoms with doses of 50-300 mg/day.

Acute dystonia
Acute dystonia (spasm torticollis, oculogyric crisis, trismus) may appear. This is reversible without discontinuation of **PRAMISUL** upon treatment with an antiparkinsonian medicine.

Tardive dyskinesia
Tardive dyskinesia that is characterized by rhythmic, involuntary movements primarily of the tongue and/or face have been reported, usually after long term administration.

d. 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. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Medicine Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9. Overdose
Experience with **PRAMISUL** in overdosage is limited. Exaggeration of the known pharmacological effects of the medicine have been reported. These include drowsiness and sedation, coma, hypotension and extrapyramidal symptoms. Fatal outcomes have been reported mainly in combination with other psychotropic medicines.

In cases of acute overdosage, the possibility of multiple medicine intake should be considered.

Since **PRAMISUL** is weakly dialysed, hemodialysis is of no use to eliminate the medicine.

There is no specific antidote to **PRAMISUL**.

Appropriate supportive measures should therefore be instituted with close supervision of vital functions including continuous cardiac monitoring due to the risk of prolongation of the QT interval until the patient recovers.

If severe extrapyramidal symptoms occur, anticholinergic medicines should be administered.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties
Other antipsychotics, ATC code: N05AX12
Pharmacological classification: A.2.6.5 Tranquilisers, miscellaneous structures.

Mechanism of action
Amisulpride binds selectively with a high affinity to human dopaminergic D2/D3 receptor subtypes whereas it is devoid of affinity for D1, D4 and D5 receptor subtypes.

Amisulpride has no affinity for serotonin, alpha-adrenergic, histamine H1 and cholinergic receptors. In addition, amisulpride does not bind to sigma sites.

In animal studies, at high doses, amisulpride blocks dopamine receptors located in the limbic structures in preference to those in the striatum.

At low doses it preferentially blocks pre-synaptic D2/D3 receptors, producing dopamine release responsible for its disinhibitory effects.

This pharmacological profile explains the clinical efficacy of amisulpride against both negative and positive symptoms of schizophrenia.

5.2. Pharmacokinetic properties

Absorption
In man, amisulpride shows two absorption peaks: one which is attained rapidly, one hour post-dose and a second between 3 and 4 hours after administration. Corresponding plasma concentrations are 39 ± 3 and 54 ± 4 ng/mL after a 50 mg dose. Absolute bioavailability is 48 %.

A carbohydrate rich meal (containing 68 % fluids) significantly decreases the AUCs, T_{max} and C_{max} of amisulpride but no changes were seen after a high fat meal. However, the significance of these findings in routine clinical use is not known

Distribution
The volume of distribution is 5.8 L/kg, plasma protein binding is low (16 %).

Biotransformation
Amisulpride is weakly metabolised: two inactive metabolites, accounting for approximately 4 % of the dose, have been identified. There is no accumulation of amisulpride and its pharmacokinetics remain unchanged after the administration of repeated doses.

Elimination
Amisulpride is eliminated unchanged in the urine. Fifty percent of an intravenous dose is excreted via the urine, of which 90 % is eliminated in the first 24 hours. Renal clearance is in the order of 20 L/h or 330 mL/min. The elimination half-life of amisulpride is approximately 12 hours after an oral dose.

Special Populations

Hepatic insufficiency
Since the medicine is weakly metabolised a dosage reduction should not be necessary in patients with hepatic insufficiency

Renal insufficiency
The elimination half-life is unchanged in patients with renal insufficiency while systemic clearance is reduced by a factor of 2.5 to 3. The AUC of amisulpride in mild renal failure increased two-fold and almost tenfold in moderate renal failure (see section 4.2). Experience is however limited and there is no data with doses greater than 50 mg.

Amisulpride is very weakly dialysed.

PRAMISUL is eliminated by renal route. In renal insufficiency, the dose should be reduced to half in patients with creatinine clearance (CR_{CL} between 30-60 mL/min and to a third in patients with CR_{CL} between 10-30 mL/min. As there is no experience in patients with severe renal impairment (CR_{CL} < 10 mL/min), these patients should not receive **PRAMISUL**.

Elderly
Limited pharmacokinetic data in elderly subjects (> 65 years) show that a 10-30 % rise occurs in C_{max}, $T_{1/2}$ and AUC after a single oral dose of 50 mg. No data is available after repeat dosing.

5.3 Preclinical safety data
An overall review of the completed safety studies indicates that amisulpride is devoid of any general, organ-specific, teratogenic, mutagenic or carcinogenic risk.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Lactose monohydrate
Methylcellulose
Microcrystalline cellulose
Croscarmellose sodium
Magnesium stearate

6.2. Incompatibilities
Not applicable

6.3. Shelf life
24 months

6.4. Special precautions for storage
Store at or below 25 °C.
Keep blisters in carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

6.5. Nature and contents of container

Blister pack:

PVC with aluminium foil:
Tablets are packed in clear 250 micron PVC film as the forming material and 25 micron aluminium foil with 7 g/m^2 heat seal lacquer as the lidding material.

Pack size: 30's - Each carton contains 3 blisters of 10 tablets each.

PVC/PVdC with aluminium foil:
Tablets are packed in clear 250 micron PVC film coated with 60 g/m^2 PVdC as the forming material and 25 micron aluminium foil with 7 g/m^2 heat seal lacquer as the lidding material.

Pack size: 30's - Each carton contains 3 blisters of 10 tablets each.

6.6. Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements for the disposal and handling of **PRAMISUL**.

7. NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
Aurogen South Africa (Pty) Ltd
Woodhill Office Park, Building 1, First floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

8. REGISTRATION NUMBER

PRAMISUL 50 mg: 52/2.6.5/0418
PRAMISUL 200 mg: 52/2.6.5/0419

9. DATE OF FIRST AUTHORISATION
10 August 2021

DETACH BEFORE DISPENSING

PATIENT INFORMATION LEAFLET

S5

PRAMISUL 50 mg (tablet)
PRAMISUL 200 mg (tablet)
Amisulpride
Contains sugar: 50 mg and 200 mg of lactose respectively.

Read all of this leaflet carefully before you start taking PRAMISUL.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- **PRAMISUL** 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 **PRAMISUL** is and what it is used for.
2. What you need to know before you take **PRAMISUL**.
3. How to take **PRAMISUL**.
4. Possible side effects.
5. How to store **PRAMISUL**.
6. Contents of the pack and other information.

1. What PRAMISUL is and what it is used for
PRAMISUL contains a medicine called amisulpride. This belongs to a group of antipsychotic medicines.
PRAMISUL is used to treat acute and chronic schizophrenia. Schizophrenia is a mental health disorder that can make you have strange and frightening thoughts, or feel, see or hear things which do not exist.

2. What you need to know before you take PRAMISUL
Do not take PRAMISUL:
- If you are allergic to **PRAMISUL** or any of the ingredients of **PRAMISUL** as listed in section 6.
- If you are taking other medicines that may cause or increase the risk of getting Torsades de Pointes (a type of abnormal heart rhythm) or prolong the QT – interval; such medicines are quinidine disopyramide, amiodarone and sotalol (medicines used to treat abnormal heart rhythms)
- If you have breast cancer or any of the following tumours: prolactin dependent tumours, adrenal gland tumour
- If you are younger than 15 years of age
- If you are breastfeeding
- If you are pregnant or plan to become pregnant
- If you are a woman of childbearing potential and you are not using adequate contraception
- If you suffer from severe kidney problems
- If you are undergoing treatment with medicine such as bepridil, cisapride, sultopride (an antipsychotic), thioridazine, methadone, IV erythromycin, IV vincamine (used to treat high blood pressure), halofantrine and pentamidine, sparfloxacin
- If you are undergoing treatment with levodopa (used to treat Parkinson's disease).

Warnings and precautions
Talk to your doctor before taking **PRAMISUL.**

Special care should be taken with PRAMISUL:
- This class of medicine can cause a syndrome called Neuroleptic Malignant Syndrome, a potentially fatal complication that is characterized by higher body temperature than normal, muscle rigidity (stiffness of muscles), self-instability, altered consciousness and high blood levels of creatinine phosphokinase (CPK, an enzyme found in the body). In the event of high body temperature, particularly with high daily doses, all antipsychotic medicines including **PRAMISUL** should be discontinued
- Hyperglycaemia has been associated with this class of medicine, therefore if you suffer from diabetes mellitus or have any risk factors for diabetes your blood sugar levels must be monitored
- If you are being treated for abnormal blood clotting disorder (thromboembolism)
- if you are over the age of 65 years
- If you are being treated for epilepsy (fits) **PRAMISUL** may cause you to have more seizures
- If you are a dementia patient
- If you abruptly stop using **PRAMISUL**, you may suffer from withdrawal symptoms (See "**If you stop taking PRAMISUL**)
- If you suffer from cardiovascular disease.

Other medicines and PRAMISUL
Always tell your healthcare professional if you are taking any other medicine. (This includes all complementary or traditional medicines).

Before taking **PRAMISUL**, tell your doctor if you are taking any of the following medicines. This is because it can increase the chance of you getting side-effects, when taken with **PRAMISUL**.

The following combinations are contraindicated:
- **PRAMISUL** increases the risk of dysrhythmia (abnormal rate of muscle contraction) if it is given with medicines like:
  - Bepridil (used to treat chest pain)
  - Cisapride (used to treat gastro oesophagael reflux disease),
  - Thioridazine (used to treat schizophrenia)
  - Erythromycin (an antibiotic used for infections)
  - Methadone (used to treat opioid dependence and chronic pain)
  - Halofantrine (used to treat malaria)
  - Pentamidine (used to treat or prevent pneumonia)
  - Sparfloxacin (an antibiotic for infections)
  - Quinidine and disopyramide, (used to treat abnormal heart rhythms)
  - Amiodarone and sotalol, (used to treat abnormal heart rhythms)
  - A group of medicines called beta blockers or calcium channel blockers (used to treat high blood pressure)
  - clonidine (used to treat high blood pressure), digoxin (used to treat heart failure), guanfacine (used to treat anxiety)
  - lithium (used to treat depression)
  - Medicines which could cause an electrolyte imbalance or hypokalaemia (low potassium levels in the blood). Examples of these products include diuretics (water tablets), laxatives, amphotericin B (used to treat fungal infections), glucocorticoids (steroids)
  - Antihistamines such as astemizole and terfenadine (used to treat allergies)
  - Mefloquine (used to treat malaria).
- **PRAMISUL** and levodopa: **PRAMISUL** produces the opposite effect to the Parkinson's medicine.

The following combinations require precautions for use:
Concomitant use of the following and **PRAMISUL** can lead to an enhanced effect:
- CNS depressants (medicines causing sedation) including narcotics (used to treat pain), anaesthetics (used to induce anaesthesia), analgesics (used to treat pain), sedative H1 antihistamines (used for allergies), barbiturates (used to treat anxiety and insomnia), benzodiazepines and other anxiolytic medicines (used to treat anxiety and insomnia).
- Medicines that are used to treat high blood pressure, and other medicines that cause low blood pressure.

PRAMISUL with food, drink and alcohol
PRAMISUL may enhance the effects of alcohol, therefore alcohol should not be consumed during treatment.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **PRAMISUL**.

You should not use **PRAMISUL** if you are pregnant or breastfeeding.

You should ensure that you always use effective contraception while you are taking **PRAMISUL**.

PRAMISUL may produce adverse effects in new born babies.

Driving and using machines
You may feel less alert, drowsy or sleepy while taking **PRAMISUL**. If this happens, do not drive or operate any heavy machinery.

PRAMISUL contains lactose

PRAMISUL contains lactose, which is a type of sugar. Before taking **PRAMISUL** please consult your doctor for advice if you have an intolerance to some sugars.

3. How to take PRAMISUL

Do not share medicines prescribed for you with any other person. Always take **PRAMISUL** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

PRAMISUL should be ingested by mouth.

The dosage should be adjusted to the intensity of mental disorder. The usual dose is once daily at oral doses up to 400 mg, higher doses should be dministered twice daily.

For acute schizophrenia patient:
Oral dose between 400 – 800 mg/day are recommended.

Your doctor will tell you how long your treatment with **PRAMISUL** will last. If you have the impression that the effect of **PRAMISUL** is too strong or too weak, talk to your doctor or pharmacist.

If you take more PRAMISUL than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.
Drowsiness (sleepy state), sedation (state of reduced excitement), coma (deep and often prolonged unconsciousness), low blood pressure and extrapyramidal symptoms may appear in overdose case. Extrapyramidal symptoms may include feeling restless or shaky, rigid muscles, feeling drowsy or sleepy which could lead to a loss of consciousness. Fatal outcomes have been reported mainly in combination with other psychotropic medicines (antidepressants, antipsychotics, mood stabilizers).

If extrapyramidal symptoms may appear you should take anticholinergic medicines (i.e., atropine).

Overdose condition, symptomatic and supportive treatment should be given.

Please note haemodialysis is not suitable for **PRAMISUL** overdose.

If you forget to take PRAMISUL
If you forgot to take a dose, take it as soon as you remember unless it is nearly time for your next dose. Do not take a double dose to make up for forgotten individual doses.

If you stop taking PRAMISUL
Acute withdrawal symptoms including nausea, vomiting and insomnia (sleepless ness) have been described after sudden stopping of high doses of mental disorder medicines. You may also suffer from a recurrence of psychotic symptoms due to involuntary movement disorders. These disorders can be akathisia, dystonia and dyskinesia (inability to sit still or inability to control movements or uncontrolled twisting of body parts).
Therefore, gradual withdrawal of **PRAMISUL** is advisable.

4. Possible side effects

PRAMISUL can have side effects.

Not all side effects reported for **PRAMISUL** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **PRAMISUL**, please consult your healthcare provider for advice.

If any of the following happen, stop taking **PRAMISUL** and tell your doctor immediately or go to the casualty department at your nearest hospital:
- Allergic reaction
- Bradycardia (slower than usual heartbeat)
- Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- Rash or itching with blisters

These are very serious side effects. If you have them, you may have had a serious reaction to **PRAMISUL**. You may need urgent medical attention or hospitalization.

Tell your doctor if the following side effects occur frequently:
- Constipation
- Nausea
- Vomiting
- Dry mouth
- Tremor (shaking of hands or feet)
- Rigidity (physical property of being stiff and resisting bending)
- Hypersalivation (abnormally high saliva secretion)
- Akathisia (feeling restless or shaky, rigid muscles, feeling drowsy or sleepy which could lead to the need to move about constantly)
- Hypokinesia (loss of partial or complete muscle movement)
- Dyskinesia (impairment of voluntary movement)
- Weight gain

The following side effects occur less frequently:
- Increase in serum prolactin levels
- Galactorrhoea (excessive or spontaneous flow of milk irrespective of nursing)
- Gynaecomastia (excessive growth of the breasts in males)
- Swollen breasts
- Erectile dysfunction (impotence)
- Hyperglycaemia (increased concentration of glucose in the blood)
- Insomnia (sleeplessness)
- Anxiety
- Agitation
- Orgasmic dysfunction (difficulty reaching orgasm)
- Dystonia (muscles contractions is uncontrollable)
- Torticollis (an unnatural condition in which the head leans to one side because the neck muscles on that side are contracted)
- Oculogyric crisis (prolonged involuntary upward deviation of the eyes)
- Trismus (prolonged spasm of the jaw muscles)
- Low blood pressure

The following side effects frequency cannot be determined:
- Leukopenia, neutropenia and agranulocytosis (abnormal low levels of white blood cells)
- Increase in blood sugar levels
- Tardive dyskinesia characterised by rhythmic, involuntary movements primarily of the tongue and/or face
- Elevation of hepatic enzymes, mainly transaminases
- Involuntary movements primarily of the tongue
- Confusion
- Neuroleptic malignant syndrome (see **Special care should be taken with PRAMISUL**)
- QT interval prolongation, (abnormal change in the heart pattern when measured on the ECG)
- Ventricular arrhythmia (abnormal rate of muscle contractions in the heart ventricles)
- Venous thromboembolism (occlusion of a blood vessel by an embolus that has broken away from a thrombus)
- Pulmonary embolism (blockage of the arteries by blood clot)
- Increase in blood cholesterol levels

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

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of **PRAMISUL**.

5. How to store PRAMISUL
Store at or below 25 °C.

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What PRAMISUL contains
The active substance is amisulpride 50 mg and 200 mg.
The other ingredients are:
Lactose monohydrate
Methylcellulose
Microcrystalline cellulose
Croscarmellose sodium
Magnesium stearate

What PRAMISUL looks like and contents of the pack

PRAMISUL 50 mg:
White to off-white, round shaped uncoated tablets with break line on one side and marking "L 73" on other side.

PRAMISUL 200 mg:
White to off-white, round shaped uncoated tablets with break line on one side and marking "L 75" on other side.

Blister pack:

PVC with aluminium foil:
Tablets are packed in clear 250 micron PVC film as the forming material and 25 micron aluminium foil with 7 g/m^2 heat seal lacquer as the lidding material.

Pack size: 30's - Each carton contains 3 blisters of 10 tablets each.

PVC/PVdC with aluminium foil:
Tablets are packed in clear 250 micron PVC film coated with 60 g/m^2 PVdC as the forming material and 25 micron aluminium foil with 7 g/m^2 heat seal lacquer as the lidding material.

Pack size: 30's - Each carton contains 3 blisters of 10 tablets each.

Holder of Certificate of Registration
Aurogen South Africa (Pty) Ltd
Woodhill Office Park, Building 1, First floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12
1448, Johannesburg
South Africa

Registration number

PRAMISUL 50 mg: 52/2.6.5/0418
PRAMISUL 200 mg: 52/2.6.5/0419

This leaflet was last revised in:
10 August 2021

Professionele Inligting oor Medisyne vir Menslike Gebruik

SKEDULERINGSTATUS

S5

1. NAAM VAN DIE MEDISYNE
PRAMISUL 50 mg (tablette)
PRAMISUL 200 mg (tablette)

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING

PRAMISUL 50 mg:
Elke tablet bevat 50 mg amisulpried
Eksipiënte met bekende effek: laktosemonohidraat 50,0 mg.

PRAMISUL 200 mg:
Elke tablet bevat 200 mg amisulpried
Eksipiënte met bekende effek: laktosemonohidraat 200,0 mg.
Vir die volledige lys van eksipiënte, verwys na afdeling 6.1

3. FARMASEUTIESE VORM

PRAMISUL 50 mg
Wit tot afwit, ronde, onbedekte tablette met 'n breeklyn aan die een kanten "L 73" aan die ander kant gedruk.
Wit tot afwit, ronde, onbedekte tablette met 'n breeklyn aan die een kant en "L 75" aan die ander kant gedruk.

4. KLINIESE BESONDERHEDE

4.1 Terapeutiese indikasies

PRAMISUL word aangedui vir die behandeling van pasiënte met akute of chroniese skisofrenie, insluitende pasiënte wat met predominante simptome gekenmerk word.

4.2 Posologie en metode van toediening
Posologie
Geen spesifieke titrering is nodig met **PRAMISUL** nie en dosisse behoort volgens individuele respons aangepas te word.
Dosisse van tot soveel as 400 mg per dag kan daagliks toegedien word, hoër dosisse twee keer per toegedien te word

Vir akute skisofrenie:
Orale dosisse van 400 - 800 mg /dag word aanbeveel. In indiwiduele gevalle mag die dosis tot 1200 mg/verhoog word. Dosisse van meer as 1200 mg/dag is weens veiligheid nie geëvalueer nie en behoort daarom nie toegedien te word nie.

Vir pasiënte metgemengde positiewe en negatiewe simptome:
Dosisse behoort aangepas te word om optimale beheer van positiewe simptome te verkry. Die onderhoudsdosis behoort indiwidueel met die minimum effektiewe dosis vasgestel te word.

Vir pasiënte gekenmerk met predominante negatiewe simptome:
Dosisse van 50 - 100 mg/dag word aanbeveel.
Dosisse behoort indiwidueel aangepas te word.

Bejaardes:
Besondere sorg behoort aan die dag gelê te word weens 'n moontlike ririko van hipotensie of sedering.
Ontoereikende lewerfunksie: Alhewel **PRAMISUL** swak gemetaboliseer word, behoort 'n laer dosis nie nodig te wees nie.

Ingekorte nierfunksie:
PRAMISUL word hoofsaaklik deur die niere opgeruim. In die geval van ontoereikende nierfunksie, behoort die dosis tot die helfte verminder te word in pasiënte met kreatiniensuiwering(CrCL) van 30 - 60 m/ml/min en tot 'n derde in pasiënte met CrCl van 10 - 30 ml/min (Sien afdeling 4.4).
Aangesie daar geen ondervinding bestaan in pasiënte met erg ontoereikende nierfunksie nie (CrCl < 10 ml/min.), behoort hierdie pasiënte nie **PRAMISUL** te ontvang nie.

Metode van toediening
Vir orale gebruik.

4.3 Kontra-indikasies

PRAMISUL word teenaangedui in:
- Hipersensitiwiteit teen amisulpried of enige van die bestanddele van **PRAMISUL** gelys in afdeling 6.1.
- Gevalle van die meegaande gebruik van ander medisyne wat die risiko van torsades de pointes, en/of verlenging van die QT-interval mag induseer of vererger (sien afdeling 4.4 en 4.5).
- Kongenitale verlenging van QT-verlenging.
- Die meegaande gebruik van prolaktienafhanklike tumore bv. pituitêre klier prolaktinome en borskanker.
- Feochromositoom.
- Swangerskap en laktasie (sien afdeling 4.6).
- Kinders jonger as 15 jaar oud.
- Vroue wat mag swanger raak, tensy hulle voldoende voorbehoeding gebruik.
- Erg ontoereikende nierfunksie (sien afdeling 4.2).
- Kombinasie met die volgende medisyne wat torsades de pointes kan induseer, soos:
  - Klas IA antidisritmiese medisyne soos klinidiendisopiramied.
  - Klas III antidisritmiese medisyne soos amiodaroon en sotalol
- Ander medisyne soos bipradiel, kisapried, sultopried, tioridasien, metadoon, IV eritromisien, IV vinkamien, halofantrien, pentamidien, sparfloksasien (sien afdeling 4.5).
- Kombinasie met levodpa (sien afdeling 4.5)

4.4 Spesiale waarskuwings en voorsorgsmaatreëls

Neuroleptiese kwaadaardige sindroom
Neuroleptiese kwaadaardige sindroom, 'n Potensieel fatale komplikasie, gekenmerk deur hipertermie, spierstyfheid, outonome onstabiliteit, verandering in bewussyn en 'n toename in kreatienfosfokinase (CPK) mag voorkom. In die geval van hipertermie, veral met hoë daaglikse dosisse, behoort alle antipsigotiese middels, insluitende **PRAMISUL**, onttrek te word.

Hiperglukemie
Hiperglukemie, in sommige gevalle ekstreem en met ketoasidose, of hiperosmolare koma of dood is met sommige is met sommige atipiese antipsigotiese middels aangemeld geassosieer. Pasiënte met 'n vasgestelde diagnose van diabetes mellitus wat op **PRAMISUL** begin word, behoort gereeld vir die agteruitgang van glukosebeheer gemonitor te word. Pasiënte met risikofaktore vir diabetes mellitus (bv. vetsug, familiële geskiedenis van diabetes)Wat op behandeling met **PRAMISUL** begin word, behoort vir simptome van hiperglukemie, insluitende polidipsie, poliürie, polifagie en swakheid gemonitor te word. Pasiënte wat simptome van hiperglukemie gedurende die behandeling met **PRAMISUL** ontwikkel, behoort vastende bloedglukosetoetsing te ondergaan. Sommige pasiënte mag egter voortsetting van antidiabetiese behandeling benodig, ongeag staking van die verdagte medisyne.

Ontoereikende nierfunksie
PRAMISUL word deur die niere opgeruim. In die geval van ontoereikende nierfunksie behoort die dosis verminder te word of afwisselende behandeling kan oorweeg word (sien afdeling 4.2)

Stuipaanvalle
PRAMISUL mag die drumpelwarde vir stuipaanvalle verlaag. Daarom behoort pasiënte met 'n geskiedenis van epilepsie noukeuring gedurende terapie met **PRAMISUL** gemonitor te word.

Bejaardes
PRAMISUL behoort weens 'n moontlike risiko van hipotensie of sedering met spesiale sorg in bejaardes. Weens ontoereikende nierfunksie mag 'n laer dosering ook nodig wees.

Parkinson se siekte
Sorg behoort aan die dag gelê te word wanneer **PRAMISUL** aan pasiënte met Parkinson se siekte toegedien word aangesien dit die siekte mag vereger. **PRAMISUL** behoort slegs gebruik te word wanneer neuroleptiese behandeling nie vermy kan word nie.

Akute onttrekkingsimptome
Akute onttrekkingsimptome, insluitende naarheid, braking en slaaploosheid is aangemeld na die vinnige staking van hoë dosisse van antipsigotiese medisyne. Die terugkeer van psigotiese simptome mag ook voorkom, en die ontwikkeling van onwillekeurige bewegingsafwykings (soos akatisie), distonie en diskinesie) is met **PRAMISUL** aangemeld (sien afdeling 4.8) Daarom word die geleidelike onttrekking van **PRAMISUL** aanbeveel.

Verlenging van die QT-interval
Sorg behoort aan die dag gelê te word wanneer **PRAMISUL** aan pasiënte met 'n bekende kardiovaskulêre siekte of 'n familiële geskiedenis van QT-verlenging het, voorgeskryf word. **PRAMISUL** induseer 'n dosisafhanklike verlenging van die QT-interval (sien afdeling 4.8). Dit is bekend dat hierdie effek die risiko van ventrikulêre disritmieë soos torsade de pointes potensieer. Voor enige toediening, en indien moontlik volgens die pasiënt se kliniese status, word daar aanbeveel om die volgende faktore wat die voorkoms van hierdie ritme kan bevoordeel, uit te sluit:
- Bragikardie van minder as 55 spm
- Hartsiekte of familiële geskiedenis van skielike dood of QT verlenging
- Elektrolietwanbalans, veral hipokalemie
- Kongenitale verlenging van die QT-interval
- Voortgaande behandeling met medisyne wat waarskynlik erge bragikardie (< 55 spm) sal veroorsaak, hipokalemie, afname in intrakardiese geleiding of verlenging van die QT-interval (sien afdeling 4.5)

Die basislyn EKG behoort voor behndelinginalle pasiënte, veral inn bejaardes en pasiënte positiewe persoonlike of familiële geskiedenis van hartsiekte of abnormale bevindings tydens kliniese hartondersoek. Gedurende terapie behoort die behoefte aan 'n EKG op 'n indiwiduele pasiëntbasis gebaseer te word.Die dosis van **PRAMISUL** behoort verlaag te word as die QT-interval te lank is en gestaak w ord wanneer die QTc > 500ms is. Periodiese elektrolietmontitering word aanbeveel, veral as die pasiënt diuretika gebruik of selfs gedurende die huidige siekte.

Die gelyktydige gebruik saam met antipsigotika behoort vermy te word (sien afdeling 4.5).

Beroerte:
In ewekansige kliniese proewe versus plasebostudies in 'n populasie van bejaarde pasiënte met demensie en wat met sekere atipiese antipsigotiese medisyne behandel is, is 'n drievoudige toename in die risiko van serebrovaskulêre gebeurtenisse waargeneem. Die meganisme van so 'n toename in risiko is nie bekend nie. 'n Toename van risiko met ander antipsigotiese middels, of ander populasies of pasiënte kan nie uitgesluit word nie. **PRAMISUL** behoort met sorg in pasiënte risikofaktore vir beroerte gebruik te word.

Bejaarde pasiënte met demensie:
Bejaarde pasiënte met demensieverwante psigose wat met antipsigotiese middels behandel word, het 'n groter risiko vir dood. Alhoewel die oorsake van dood in kliniese proewe met atipiese antipsigotika gewissel het, het dit gelyk asof die grootste aantal sterftes kardiovaskulêr (bv. hartversaking, skielike dood) of besmetlik (bv. pneumonie) van aard was. Uit waarnemingstudies wil dit voorkom, netsoos met atipiese antipsigotiese medisyne, asof behandeling met konvensionele antipsigotiese medisyne, die mortaliteit mag verhoog.

PRAMISUL is nie vir die gebruik van demensieverwante gedragsafwykings geregistreer nie.

Veneuse tromboëmbolisme (VTE)

Gevalle van VYE is met antipsigotiese medisyne aangemeld. Aangesien pasiënte wat met antipsigotika behandel word dikwels met verworwe risikofaktore vir VTE presenteer, behoort alle risikofaktaore vir VTE geïdentifiseer te word voor en gedurende die gebruik van **PRAMISUL,** en behoort voorsorgsmaatreëls getref te word.

Borskanker
PRAMISUL mag prolaktienvlakke verhoog Daarom behoort sorg aan die dag gelê te word in pasiënte met 'n geskiedenis of familiëlegeskiedenis van borskanker gedurende terapie met **PRAMISUL** en behoort noukeurig gedurende terapie met **PRAMISUL** gemonitor te word.

Bloedddiskrasieë
Leukopenie, neutropenie en agranulositose is met antipsigotika, insluitende **PRAMISUL**, aangemeld. Onverklaarbare infeksies of koors mag bewys wees van boedddiskrasieë (sien afdelinfg 4.8) en vereis onmiddellike hematologiese ondersoek.

Laktose
Pasiënte met die skaars oorerflike probleem van onverdraagbaarheid van galaktose, die Laplandse laktasetekort of wanabsorpsie van glukose/galaktose, moet nie **PRAMISUL** gebruik nie.

4.5 Interaksie met ander medisyne en ander vorms van interaksie

Teenaangeduide kombinasies
- Medisyne wat torsade de pointes kan induseer:
  - Klas IA antidisritmiese middels soos kinidien en disopiramied
  - Klas III antidisritmiese middels soos amiodaroon en sotalol
  - Ander medisyne soos bepridiel, kisapried, sultopried, tioridasien, metadoon, eritromisien (intraveneuse toediening), vinkamien (intraveneuse toediening) halofantrien, pantamidien, sparfloksasien, asool swamweerders (sien afdeling 4.3).
- Levodopa: wedersydse antagonisme van effekte tussen levodopa en neuroleptika. **PRAMISUL** mag die effekte dopamienagoniste bv. bromokriptien en ropinirool teenwerk.

Kombinasies wat nie aanbeveel word nie
- Medisyne wat die risiko van torsade de pointes verhoog of die QT-interval kan verleng:
  - Bragikardie-induserende middels soos beta-blokkeerders, bragikardie-induserende kalsiumkanaalblokkeerders soos diltiasem en verapamiel, klonidien, guanfasien en digitalis
  - Medisyne wat hipokalemie elektrolietwanbalans induseer soos Hipokalemiese diuretika, stimulerende lakseermiddels, amfoterisien B (intraveneuse toediening), glukokortikoïede en ketrakosaktides Hipokalemie behoort reggestel te word (sien afdeling 4.3)
  - Antipsigotika soos pimosied en haloperidol (sien afdeling 4.3)
  - Imipramien antidepressante
  - Litium
  - Sommige antihistamiene soos astemisool en terfinadien
  - Meflokien
- **PRAMISUL** mag die sentrale effekte van alkoholvererger. Daarom behoort alkohol nie gedurende terapie gebruik te word nie.

Kombinasies wat voorsorgsmaatreëls vir gebruik vereis
Die gelyktydige gebruik van die volgende middels mag tot die potensiëring van die middel lei:
- SSS depressante insluitende narkotika, anestetika, pynstillers, sedatiewe H1 antihistamiene, barbiturate bensodiasepienen en ander angsiolitiese middels, klonidien en derivate.
- Antihipertensiewe middels en ander hipotensiewe middels.

4.6 Vrugbaarheid, swangerskap en laktasie
Die veiligheid vab **PRAMISUL** gedurende swangerskap en laktasie is nie vasgestel nie.

Vroue wat moontlik swanger mag raak
Vir vroue wat moontlik swanger mag raak, behoort effektiewe voorbehoeding voor behandeling ten volle met die dokter bespreek te word.

Swangerskap
Die gebruik van **PRAMISUL** word teenaangedui in swangerskap (sien afdeling 4.3).

Neonate wat aan antipsigotika (insluitende **PRAMISUL** gedurende die derde trimester van swangerskap blootgestel loop 'n risiko van newe-effekte, insluitende ekstrapiramidale en/of onttrekkingsimptome wat in graad van erns duurte mag wissel na geboorte (sien (afdeling 4.8).Daar bestaan vermeldings van agitasie, hipertonie, hipotonie, bewerasie, slaapsug, moeite met asemhaling of voedingsafwyking. Gevolglik behoort pasgebore babas noukeurig gemonitor te word.

Laktasie
Dit is nie bekend of **PRAMISUL** in borsmelk uitgeskei word nie. Borsvoeding word daarom teenaangedui (sien afdeling 4.3).

Vrugbaarheid
In dierestudies is 'n afname in vrugbaarheidgekoppel aan die farmakologiese effekte van die medisyne (prolaktien gemedieerde effekte) waargeneem.

4.7 Vermoë om te bestuur en om met masjinerie te werk

Wanneer soos voorgeskryf word, gebruik word, veroorsaak **PRAMISUL** slaapsug wat die vermoë om te bestuur en om met swaar masjinerie te werk beperk.

4.8 Newe-effekte

a. Opsomming van die veiligheidsprofiel
Aan die begin van behandeling kom hardlywigheid, naarheid, braking en droë mond dikwels voor.
Ekstrapiramidale simptome kom ook dikwels voor: bewerasie, styfheid, hipokinesie, oormaat speeksel, akatisie en diskinesie.

b. Getabuleerde lys van newe-effekte

Orgaansisteem klas	Dikwels	Minder dikwels
Afwykings van die immuunsisteem		Allergiese reaksie
Endokriene afwykings	Galaktorree, amenorree, of menstruele afwykings, ginekomastie, borspyn of-vergroting, prolaktinomie (sien afdeling 4.3), erektiele disfunsie	
Metabolisme- en voedingsafwykings		Hiperglukemie (sien afdeling 4.4)
Psigiatriese afwykings	Slaaploosheid, angs, agitasie, orgasmiese disfunksie	
Afwykings van die senuweestelsel	Ekstrapiramidale simptome mag voorkom: bewerasie, styfheid, hipokinesie, oormaat speeksel, akatisie, diskinesie, akute distonie (spasma torticollis, okulogiriese krisis, trismus), slaapsug	Tardiewe diskinesie, gekenmerk deur ritmiese, onwillekeurige bewegings hoofsaaklik van die tong en/of gesig is aangemeld,, gewoonlik na langtermyn toediening.
Hartafwykings	Hipotensie	Bragikardie
Gastroïntestinale afwykings	Hardlywigheid, naarheid, braking, droë mond	
Algemene afwykings en kondises by die plek van toediening		Naarheid, braking, terugkeer van psigotiese simptome, ontwikkeling van onwilleurige beweginsafwykings, soos akatisie, distonie en diskinesie)(sien afdeling 4.4)
Ondersoeke	Massatoename	Verhoging van lewerensieme, hoofsaaklik transaminases

Na bemarkingsdata

	Frekwensie of voorkoms
Orgaansisteem klas	**Frekwensie onbekend**
Afwykings van die bloed- en limfsisteem	Leukopenie, neutropenie en with , agranulositose (sien afdeling 4.4)
Metabolisme- en voedingsafwyings	Hipertrigliseridemie en with , hipercholesterolemie
Psigiatriese afwykings	Verwardheid
Afwykings van die senuweestelsel	Neuroleptiese kwaadaardige sindroom (sien afdeling 4.4) wat 'n potensieel fatale komplikasie mag wees
Hartafwykings	QT-interval verlenging en ventrikulêrearritmieë soos torsade de pointes, ventrikulêre tagikardie wat tot ventrikulêre fibrillasie of hartstilstand of skielike dood mag lei.
Vaskulêre afwykings	Gevalle van veneuse tromboëmbolisme mag lei, insluitende gevalle van pulmonêre embolisme, soms fataal, en gevalle van diepaar trombose is met antipsigotiese middels aangemeld.
Afwykings van die vel en subkutane weefsel	Angioëdeem, urtikarie
Swangerskap, puerperium en perinatale kondisies	Medisyne onttrekkingsimptome en neonate (sien afdeling 4.6)

c. Beskrywing van geselekteerde newe-effekte
Toename in prolaktienvlakke
Amisulpried veroorsaak 'n toename in die prolaktienvlakke in die bloed, wat omkeerbaar is wanneer die middel onttrek word. Dit mag tot galaktorree, amenorree, menstruele afwykings, ginekomastie, borspyn of -vergroting, prolaktinoom (sien afdeling 4.3) en erektiele disfunksie lei.

Ekstrapiramidale simptome
Bewerasie, styfheid, hipokinesie, oormaat speeksel akatisie, diskinesie is gewoonlik gering teen optimale dosisse en gewoonlik omkeerbaar sonder onttrekking van **PRAMISUL** met die toediening van antiparkinsonmedikasie. Die voorkoms van ekstrpiramidale simptome wat dosisverwant is, bly baie laag in die behandeling van pasiënte met predominante negatiewe simptome met dosisse van 50 - 300 mg/dag.

Akute distonie
Akute distonie (spasma torticollis, oculogyric krisis, trismus) kan verskyn. Dit is omkeerbaar sonder staking van **PRAMISUL** by behandeling met 'n antiparkinsoniese medisyne.

Tardiewe diskinesie
Tardiewe diskinesie wat deur ritmiese, onwillekeurige bewegings hoofsaaklik van die tong en/of gesig gekenmerk word, gewoonlik na 'n lang periode van toediening.

d. Aanmelding van verdagte newe-effekte
Die aanmelding van verdagte newe-effekte van die medisyne na registrasie is belangrik. Dit laat toe vir aanhoudende monitering van die voordeel/risikobalans van die medisyne. Gesondheidsorgverskaffers word versoek om enige verdagte newe-effektte aan SAHPRA via: "**6.04 Newe-effekte Reaksie Aanmeldingsvorm**" wat aanlyn onder SAHPRA se publikasie gevind kan word: https://sahpra.org.za//Publications/Index/8.

4.9 Oordosering
Ondervindingvan oordosering met **PRAMISUL** is beperk**.** Verergering van die bekende farmakologiese effekte van die medisyne is aangemeld. Dit sluit die volgende in: lomerigheid en sedering, koma, hipotensie en ekstrapiramidale simptome. Fatale simptome is aangemeld, hoofsaaklik in kombinasie met ander psigotropiese middels
In gevalle van akute oordosering behoort die moontlikheid van veelvoudige medisyne oorweeg te word.
Aangesien **PRAMISUL** swak gedialiseer word, is hemodialise van geen nut om hierdie medisyne te elimineer nie.
Daar is gee spesifieke teenmiddel vir **PRAMISUL** nie.

Toepaslike ondersteunende maatreëls behoort ingestel te word met noukeurige monitering van lewenstekens, insluitende aanhoudende hartmonitering weens die risiko van verlenging van die QT-interval totdat die pasiënt herstel.
As erge ekstrapiramidale simptome behoort antichlinergiese medisyne toegedien word.

5 FARMAKOLOGIESE EIENSKAPPE

5.1 Farmakodinamiese eienskappe
Ander antipsigotika, ATC code: N05AX12
Farmakologiese klassifikasie: A.2.6.5 Kalmeermiddels, ander strukture

Meganisme van werking
Amisulpried bind selektiewelik met 'n hoë affiniteit aan menslike dopaminergiese D2/D3 reseptor sub-tipes terwyl dit geen affiniteit vir D1, D4, en D5 reseptor sub-tipes het nie.
Amisulpried het geen affiniteit vir serotonien, alfa-adrenergiese, histamien H1 en cholinergiese reseptors nie. Boonop bind amisulpried nie aan sigmabindingsplekke nie.
Teen hoë dosisse in dierestudiesblok amisulpried die dopaminreseptorsin die limbiese strukture eerder as dié in die striatum.
Teen lae dosisse blokkeer dit eerder die pre-sinaptiese D2/D3 reseptors wat dan dopamien vrystel wat tot sy disinhibitoriese effek lei.
Die farmakologiese profielverduidelik die kliniese effektiwiteit van amisulpried teen beide negatiewe en positiewe simptome van skisofrenie

5.2 Farmakokinetiese eienskappe

Absorsie
In die mens toon amisulpried twee absorpsiepieke, en wat vinnige bereik word, een uur na dosering en 'n tweede een tussen 3 en 4 ure na toediening. Ooreenstemmende plasmakonsentrasies is 39 ±4 ng/ml en ±4 ng/ml na 'n dosis van 50 mg. Die absolute biobeskikbaarheid is 48 %'n Koolhidraatryke maaltyd bevattende 65 % vog het die AOKs, T_{maks}, K_{maks} van amisulpried aansienlik verminder, maar geen veranderingeis is in 'n hoë-vet maaltyd waargeneem nie. Die noemenswaardigheid van hierdie bevindings in die kliniese roetine is egter nie bekend nie.

Verspreiding
Die volume van verspreiding is 5,8 L/kg, plasmabinding is laag (16 %)

Biotransformasie
Amisulpried word swak gemetaboliseer: Twee onaktiewe metaboliete wat ongeveer 4 % van die dosis opmaak, is geïdentifiseer. Daar vind geen akkumulasie van amisulpried plaas nie en sy farmakokinetika bly onveranderd na die toediening van herhaalde dosisse.

Opruiming
Amisulpried word onveranderd in die urien uitgeskei. Vyftig persent van 'n intraveneuse dosis word in die urien uitgeskei, waarvan 90 % binne die eerste uur plaasvind. Nieropruiming is in die orde van 20 L/h of 330 mL/min. Die opruimingshalfleeftyd van amisulpried is ongeveer 12 ure na 'n enkel mondelikse dosis.

Spesiale populasies

Ontoereikende lewerfunksie
Aangesien die medisyne swak gemetaboliseer word, behoort 'n afname in dosis nie nodig te wees in die geval van ontoereikende lewerfunksie nie.

Ontoereikende nierfunksie
Die eliminasiehalfleeftyd bly onveranderd in pasiënte met ontoereikende nierfunksie terwyl sistemiese opruiming met 'n faktor van 2,5 tot 3 afneem. Die AOK van amisulpried in gering ontoereikende nierfunksie neem tweevoudig en byna tienvoudig toe matig ontoereikende nierfunksie (sien afdeling 4.2). Ondervinding is egter beperk en daar bestaan geen data met dosisse van meer as 50 mg nie.
Amisulfied word baie swak gedialiseer.

PRAMISUL word deur die niere uitgeskei. In gevalle van ontoereikende nierfunksie behoort die dosis na die helfte in pasiënte met kreatinien-opruiming (CR_{CL} tussen 30 - 60 mL/ en na 'n derde in pasiënte met tussen 10-30 mL/min verminder te word. Aangesien daar geen ondervinding in pasiënte met nieropruiming (CR_{CL} < 10 mL/min) bestaan nie, behoort **PRAMISUL** nie aan hierdie pasiënte toegedien te word nie.

Bejaardes
Beperkte farmakokinetiese dat in bejaarde pasiënte (> 65 jaar ou) toonnaan dat 'n 10-30 % verhoging in K_{maks}, $T_{1/2}$ en AOK na 'n enkel dosis van 50 mg voorkom. Geen data is beskikbaar na herhaalde dosering nie.

5.3 Prekliniese veiligheidsdata
'n Alghele oorsig van ndie voltooidem veiligheidstudies toon aan dat amisulpried geen algemene, organnspesifieke,teratogeniese, mutageniese of nkarsinogeniese effek toon nie.

6 FARMASEUTIESE BESONDERHEDE

6.1 Lys van eksipiënte
Laktosemonohidraat
Metielsellulose
Mikrokristallyne sellulose
Kroskarmellose natrium
Magnesiumstearaat

6.2 Onversoenbaarhede
Nie van toepassing nie.

6.3 Rakleeftyd
24 maande

6.3 Spesiale voorsorgsmaatreëls vir opberging
Bewaar teen of benede 25 °C
Hou die stolpstrokies in die karton totdat dit benodig word.

HOU BUITE BEREIK VAN KINDERS

6.4 Aard en inhoud van die houer

Stolpverpakking

PVC met aluminiumfoelie
Tablette word in held 250 mikron PVC film as die vormingsmateriaal en 25 mikron aluminiumfoelie met 7 g/m[2] hittegeseëlde lak as dekkingsmateriaal verpak.

Pakgrootte: 30s - Elke karton bevat 3 stolpstrokies van 10 tablette elk.

PVC/PVdC
Tablette word in held 250 mikron PVC film as die vormingsmateriaal en 60 mikron aluminiumfoelie met 7 g/m[2] hittegeseëlde lak as dekkingsmateriaal verpak.

Pakgrootte: 30s - Elke karton bevat 3 stolpstrokies van 10 tablette elk.

6.5 Spesiale voorsorgsmaatreëls vir die wegdoen van ongebruik medisyne of afvalmateriaal van hierdie medisyne en ander hantering van die produk
Geen spesiale vereistes vir die wegdoen en hantering van **PRAMISUL** is nodig nie

7. HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE EN VERVAARDIGER
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Johannesburg
Suid Afrika

8. Registrasienommer
PRAMISUL 50 mg: 52/2.6.5/0418
PRAMISUL 200 mg: 52/2.6.5/0419

9. DATUM VAN EERSTE GOEDKEURING
10 Augustus 2021

P1528654

DETACH BEFORE DISPENSING

PASIËNTINLIGTINGSBLAD

S5

PRAMISUL 50 mg (tablette)
PRAMISUL 200 mg (tablette)
Amisulpried
Bevat suiker: 50 mg en 200 mg laktose, respektiewelik.

Lees die hele inligtingsblad noukeurig voordat u begin om PRAMISUL te neem
- Hou hierdie inligtingsblad. U mag dit moontlik weer wil lees.
- As u enige verdere vrae het, moet u u dokter, apteker, verpleegster of ander professionele gesondheidswerker raadpleeg.
- **PRAMISUL** is vir u persoonlik voorgeskryf en u behoort nie u medisyne met ander deel nie, ookal toon hulle dieselfde simptome as u.

Wat is in hierdie inligtingsblad.
1. Wat is in hierdie inligtingsblad en waarvoor dit gebruik word.
2. Wat u behoort te weet voordat u **PRAMISUL** neem
3. Hoe om **PRAMISUL** te neem
4. Moontlike newe-effekte
5. Hoe om **PRAMISUL** op te berg
6. Inhoud van die pak en ander inligting.

1. Wat is PRAMISUL en waarvoor dit gebruik word.
PRAMISUL bevat 'n medisyne wat amisulpried genoem word. Dit behoort aan die groep van medisyne wat antipsigotiese middels genoem word.

PRAMISUL word gebruik om akute en chroniese skisofrenie te behandel. Skisofrenie is 'n geestelike gesondheidsfawyking wat kan veroorsaak dat u vreemde en skrikwekkende gedagtes ondervind, of dinge voel of sien of hoor wat nie bestaan nie.

2. Wat u behoort te weet voordat u begin om PRAMISUL te neem

Moenie PRAMISUL neem nie:
- As u allergies teen **PRAMISUL** of enige van die bestanddele van **PRAMISUL** is nie (kyk na afdeling 6).
- As u ander medisyne neem wat die risiko vir die ontwikkeling van torsade de pointes ('n soort abnormale hartritme) mag veroorsaak of vererger, of die QT-interval mag verleng; sulke medisyne is kinidiendisopiramied, amiodaroon en sotalol (medisyne wat gebruik word om abnormale hartritme mee te behandel).
- As u aan borskanker of enige van die volgende tumors ly: prolaktien afhanklike tumor, byniertumor.
- As u jonger as 15 jaar oud is.
- As u swanger is of beplan om swanger te raak.
- As u borsvoed.
- As u moontlik swanger mag raak en nie voldoende voorbehoeding gebruik nie.
- As u aan erge nierprobleme ly.
- As u behandeling met medisyne soos bepridiel, kisapried, sultopried ('n antipsigotiese middel), tioridasien, metadoon, IV eritromisien, IV vinkamien (gebruik om bloeddruk te behandel), halofantrien en pentamidien of sparfloksasien ondergaan.
- As u behandeling met levodopa ondergaan (gebruik om Parkinson se siekte te behandel).

Waarskuwings en voorsorgsmaatreëls

Vertel u dokter voordat u **PRAMISUL** neem.

Neem spesiale sorg met **PRAMISUL**:
- Hierdie klas van medisyne kan 'n sindroom met die naam van Neuroleptiese Kwaadaardige Sindroom, 'n potensieel fatale komplikasie veroorsaak wat gekenmerk word deur hoër liggaamstemperatuur as normaal, spierstyfheid, wisselende bewussyn en hoë bloedvlakke van Kreatienfosfokinase (KPK), 'n ensiem wat in die liggaam gevind word. In die geval van hoë temperatuur, veral met hoë daaglikse dosisse, behoort alle antipsigotiese medisyne, insluitende **PRAMISUL** ontrek te word.
- Hiperglukemie is met hierdie klas medisyne waargeneem. As u daarom aan diabetes mellitus ly, of enige risikofaktore vir diabetes het, moet u bloedsuikervlakke gereeld gemonitor word.
- As u vir 'n abnormale bloedklontafwyking behandel word (tromboëmbolisme).
- As u ouer as 65 jaar oud is.
- As u vir epilepsie (stuipaanvalle) behandel word. **PRAMISUL** mag veroorsaak dat u meer aanvalle kry.
- As u aan demensie ly.
- As u ewe skielik ophou om **PRAMISUL** te gebruik, mag u onttrekkingsimptome ondervind (Sien **"As u ophou om PRAMISUL te neem"**).
- As u aan 'n kardiovaskulêre siekte ly.

Ander medisyne en PRAMISUL
Stel altyd u professionele gesondheidswerker in kennis as u ander medisyne neem. Dit sluit alle komplementêre en tradisionele medisyne in.

Voordat u **PRAMISUL** neem moet u u dokter in kennis stel as u enige van die volgende medisyne neem, aangesien dit die kans vir newe-effekte verhoog wanneer dit saam met **PRAMISUL** gebruik word.

Die volgende kombinasies word teenaangedui:
- **PRAMISUL** verhoog die risiko van disritmieë (abnormale tempo van sametrekking)) as dit saam met die volgende geneem word.
  - Bepridiel (gebruik vir borspyn)
  - Kisapried (gebruik vir gastroësofagale refluksiekte)
  - Eritromisien ('n antibiotika gebruik vir infeksies)
  - Metadoon (gebruik om opioïedafhanklikheid en chroniese pyn te behandel)
  - halofantrien (gebruik om malaria te behandel)
  - Pentamidien (gebruik om pneumonie te behandel)
  - Sparfloksasien ('n antibiotika vir infeksies)
  - Kinidien en disopiramied (gebruik om abnormale hartritmes te behandel)
  - Amiodaroon en sotalol(gebruik om abnormale hartritmes te behandel)
  - 'n Groep medisyne wat betablokkeerders of kalsiumkanaal-blokkeerders genoem word (gebruik om hoë bloeddruk te behandel)
  - Klonidien (gebruik vir hoë bloeddruk), digoksien (gebruik om hartversaking te behandel), guanfasien (gebruik om angs en hoë bloeddruk behandel)
  - Litium (gebruik om depressie te behandel)
  - Medisyne wat 'n elektrolietwanbalans of hipokalemie (lae kalsiumvlakke in die bloed) kan veroorsaak. Voorbeelde van hierdie produkte is: diuretika (watertablette), lakseermiddels, amfoteresien B inspuiting ('n swamweerder), glukokortikoïede (gebruik om allergieë te behandel)
  - Meflokien (gebruik om malaria te behandel).
- **PRAMISUL** en levodopa:" **PRAMISUL** veroorsaak teenoorgestelde effekte as middels teen Parkinson se siekte

Die volgende kombinasies vereis voorsorgsmaatreëls vir gebruik:

Die gelyktydige gebruik van die volgende en **PRAMISUL** kan tot 'n oormatige effek lei:
- SSS-depressante, insluitende narkotika (vir die gebruik teen pyn), anestetika (gebruik vir narkose), pynstiller (gebruik om pyn te behandel), sederende H1 antihistamiene (gebruik vir allergieë), barbiturate (SSS-depressante) en bensodiasepiene (gebruik om angs, stuipaanvalle en slaaploosheid te behandel)
- Medisyne wat gebruik word om hoë bloeddruk te behandel en ander middels wat lae bloeddruk veroorsaak.

PRAMISUL met voedsel, vloeistof en alkohol

PRAMISUL mag die effekte van alkohol vererger. Daarom behoort alkohol nie gedurende behandeling gebruik te word nie.

Swangerskap, borsvoeding en vrugbaarheid

As u swanger is of u baba borsvoed, moet u asseblief u dokter , apteker of professionele gesondheidswerker raadpleeg voordat u **PRAMISUL** neem.

Moenie **PRAMISUL** as u swanger is of borsvoed nie.

U moet verseker dat u altyd voldoende kontrasepsie gebruik terwyl u **PRAMISUL** neem.

PRAMISUL mag newe-effekte in pasgebore babas veroorsaak.

Bestuur en die gebruik van masjinerie

U mag lomerig en slaperig voel terwyl u **PRAMISUL** neem. As dit gebeur moet u nie motor bestuur of met masjinerie werk nie.

PRAMISUL bevat laktose

PRAMISUL bevat laktose wat 'n soort suiker is. Raadpleeg asseblief u dokter as u intolerant teen sekere suikers is.

3. Hoe om PRAMISUL te neem

Moenie medisyne wat aan u voorgeskryf is met enige ander persoon deel nie. Neem **PRAMISUL** altyd presies soos deur u dokter voorgeskryf. Raadpleeg u dokter of apteker as u onseker is.

PRAMISUL moet per mond geneem word.

Die dosis moet volgens die intensiteit van die afwyking aangepas te word. Die normale dosis is een keer per dag teen orale dosisse tot 400 mg per dag. Hoër dosisse behoort twee keer per dag toegedien te word.

Vir pasiënte met akute skisofrenie:
Orale dosisse van 400 - 800 mg/dag word aanbeveel.

U dokter sal u inlig oor hoe lank u behandeling met **PRAMISUL** sal duur. As u onder die indruk is dat die effek van **PRAMISUL** te sterk of te swak, raadpleeg asseblief u dokter of apteker.

As u te veel PRAMISUL neem

In die geval van oordosering, raadpleeg u dokter of apteker. As hulle nie beskikbaar is nie, gaan na u naaste hospitaal of gifbeheersentrum.

Lomerigheid (slaperigheid), sedering, koma (diep en dikwels verlengde bewusteloosheid), lae bloeddruk en ekstrapiramidale effekte mag in gevalle van oordosering voorkom. Ekstrapiramidale simptome sluit 'n gevoel van rusteloosheid, bewerige, stywe spiere, 'n gevoel van lomerigheid of slaperigheid insluit wat tot 'n verlies van bewussyn kan lei. Fatale uitkomste is aangemeld, hoofsaaklik in kombinasie met ander psigotropiese medisyne (antidepressante, antipiretika, kalmeermiddels) Is ekstrapiramidale simptome sou voorkom, behoort u anticholinergiese middels (bv. atropien) te neem.

Met oordosering behoort simptomatiese en ondersteunende behandeling toegedien te word.

Neem kennis dat hemodialise nie geskik vir die oordosering met **PRAMISUL** is nie.

As u vergeet het om PRAMISUL te neem

As u vergeet het om u dosis **PRAMISUL** te neem, neem dit so gou as wat u daarvan onthou, tensy dit byna tyd vir u volgende dosis is. Moenie die dosis verdubbel om vir 'n oorgeslaande dosis op te maak nie.

As u ophou om PRAMISUL te gebruik

Akute onttrekkingsimptome, insluitende naarheid, braking en slaaploosheid is aangemeld na die skielike staking van die gebruik van medisyne vir geestesafwykings. Weens die onwillekeurige mag u ook aan 'n terugkeer van die psigotiese simptome ly. Hierdie afwykings mag akatisie, distonie en diskinesie (onvermoë om stil te sit of die onvermoë om bewegings te beheer of onbeheerde rukbewegings van die liggaam.

Daarom word die geleidelike onttrekking van **PRAMISUL** aanbeveel.

4. Moontlike newe-effekte

PRAMISUL kan newe-effekte hê.

Nie al die newe-effekte wat vir **PRAMISUL** aangemeld is, word in hierdie inligtingsblad genoem nie. As u algemene gesondheid agteruitgaan of u ondervind enige newe-effek terwyl u **PRAMISUL** neem, moet u as u professionele gesondheidswerker raadpleeg.

As enige van die volgende gebeur moet u ophou om **PRAMISUL** te neem en onmiddellik u dokter raadpleeg, of gaan na die ongevalle afdeling van u naaste hospitaal:
- Allergiese reaksie
- Bradikardie (harttempo stadiger as normaal)
- Swelling van die hande, voete, enkels, gesig, lippe, mond of keel wat moeite met sluk of asemhaling mag veroorsaak
- Uitslag met jeuk of blasies

Hierdie is baie ernstige newe-effekte. As u hulle ondervind, toon u dalk 'n baie sterk reaksie teen **PRAMISUL**. U het moontlik baie dringende aandag of hospitalisering nodig.

Stel u dokter in kennis as die volgende newe-effekte dikwels voorkom:
- Hardlywigheid
- Naarheid
- Braking
- Droë mond
- Bewerasie (van die hande of voete)
- Styfheid (fisiese styfheid en onvermoë om te buig)
- Oormatige speekselvloei (oormatig hoë speekseluitskeiding)
- Akatisie (gevoel van spierbewing en 'n behoefte om die hele tyd rond te beweeg)
- Hipokinesie (Gedeeltelike of totale verlies aan die gebruik van spiere)
- Diskinesie (inkorting van willekeurige beweging)
- Massatoename

Die volgende newe-effekte kom minder dikwels voor:
- Toename in serumprolaktienvlakke
- Galaktorree (oormatige of spontane melkvloei, ongeag of die persoon borsvoed of nie)
- Ginekomastie (oormatige groei van borste in mans)
- Geswelde borste
- Erektiele disfunksie (impotensie)
- Hiperglukemie (toename in die konsentrasie van glukose in die bloed)
- Slaaploosheid (onvermoë om te slaap)
- Angs
- Agitasie
- Orgasmiese disfunksie (onvermoë om 'n orgasme te bereik)
- Distonie (onbeheerbare spierbewegings)
- Torticollis ('n abnormale kondisie waar die kop een kant toe leun as gevolg van spiere wat aan die ander kant saamtrek)
- Okulogiriese krisis
- Trismus (verlengde spasma van die kaakspiere)
- Lae bloeddruk

Die frekwensie van die volgende newe-effekte kan nie vasgestel word nie:
- Leukopenie, neutropenie en agranulositose (abnormaal lae aantal witbloedselle)
- Toename in bloedsuikervlakke
- Tardiewe diskinesie gekenmerk deur ritmiese, onwillekeurige bewegings, veral van die tong en/of gesig
- Verhoging van lewerensieme, veral transaminases
- Onwillekeurige bewegings, veral van die tong
- Verwardheid
- Neurolepties kwaadaardige sindroom (sien **Spesiale sorg behoort met PRAMISUL geneem word**)
- Verlenging van die QT-interval (abnormale verandering in die hartpatroon wanneer op 'n EKG gemeet word)
- Ventrikulêre arritmie (abnormale tempo van spiersametrekkings in die hartventrikels)
- Veneuse tromboëmbolisme (okklusie van die bloedvat deur 'n embolus wat van 'n trombus weggebreek het)
- Pulmonêre embolisme (blokkasie van die bloedvate deur 'n bloedklont)
- Toename in bloedcholesterol

A u enige newe-effekte waarneem moet u u dokter of apteker in kennis stel

Aanmelding van newe-effekte
As u newe-effekte ondervind moet u u dokter of verpleegster raadpleeg. U kan ook die newe-effekte aan SAHPRA via: "**6.04 Newe-effekte Reaksie Aanmeldingsvorm**" wat aanlyn onder SAHPRA se publikasie wat aanlyn gevind kan word: https://sahpra.org.za//Publications/Index/8. Deur newe-effekte aan te meld kan u help om meer inligting om meer onligting oor die veiligheid van **PRAMISUL** te verskaf.

5. Hoe om PRAMISUL op te berg
Bêre teen of benede 25 °C

HOU ALLE MEDISYNE BUITE BEREIK VAN KINDERS

Neem alle ongebruikte medisyne na u apteker terug.
Moenie ongebruikte medisyne in die riolering wegdoen nie (bv. toilette).

6. Inhoud van die verpakking en ander inligting

Wat PRAMISUL bevat
Die aktiewe bestanddeel is amisulpried 50 mg en 200 mg
Die ander bestanddele is:
Laktosemonohidraat
Metielsellulose
Mikrokristallyne sellulose
Kroskarmellose natrium
Magnesiumstearaat

Hoe PRAMISUL lyk en inhoud van die verpakking

PRAMISUL 50 mg
Wit tot afwit, ronde onbedekte tablette met 'n breeklyn aan die een kant en "L 73" aan die ander kant.

PRAMISUL 200 mg
Wit tot afwit, ronde onbedekte tablette met 'n breeklyn aan die een kant en "L 75" aan die ander kant.

Stolpverpakking

PVC met aluminiumfoelie
Tablette word in held 250 mikron PVC film as die vormingsmateriaal en 25 mikron aluminiumfoelie met 7 g/m[2] hittegeseëlde lak as dekkingsmateriaal verpak.

Pakgrootte: 30s - Elke karton bevat 3 stolpstrokies van 10 tablette elk.

PVC/PVdC

Tablette word in held 250 mikron PVC filmbedekte met 60 g/m[2] as die vormingsmateriaal en 25 mikron aluminiumfoelie met 7 g/m[2] hittegeseëlde lak as dekkingsmateriaal verpak.

Pakgrootte: 30s - Elke karton bevat 3 stolpstrokies van 10 tablette elk.

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PRAMISUL 50 mg: 52/2.6.5/0418
PRAMISUL 200 mg: 52/2.6.5/0419

Hierdie blad is laas hersien op:

10 Augustus 2021