For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

AMAZEO

1. Generic Name

Amisulpride Tablets I.P.

2. Qualitative and quantitative composition

Amazeo 50

Each film coated tablet contains:

Amisulpride I.P.……50 mg

Excipients……q.s.

Colour: Titanium Dioxide I.P.

Amazeo 100

Each film coated tablet contains:

Amisulpride I.P.……100 mg

Excipients……q.s.

Colour: Titanium Dioxide I.P.

Amazeo 200

Each film coated tablet contains:

Amisulpride I.P.……200 mg

Excipients……q.s

Colour: Titanium Dioxide I.P.

Amazeo 300

Each film coated tablet contains:

Amisulpride I.P.……300 mg

Excipients……q.s

Colour: Titanium Dioxide I.P.

The excipients used are Lactose Monohydrate, Microcrystalline Cellulose, Colloidal Silicon Dioxide, Polyoxyl Stearate, Hydroxy Propyl Methyl Cellulose, Sodium Starch Glycolate, Talc, Magnesium Stearate, Polyethylene Glycol, and Titanium Dioxide.

3. Dosage form and strength

Dosage form: Film coated tablet

Strength: 50, 100, 200, and 300

4. Clinical particulars

4.1 Therapeutic indication

It is indicated for acute and chronic schizophrenic disorders, in which positive and negative symptoms are prominent, including patients characterized by predominant negative symptoms, schizophrenic disorder.

4.2 Posology and method of administration

Posology

Dose: As directed by the Physician.

Positive symptoms:

For acute psychotic episodes, a daily dose between 400 mg and 800 mg is recommended.

In individual cases, the daily dose may be increased up to 1200 mg. Doses above 1200 mg/day have not been extensively evaluated for safety and therefore should not be used.

No specific titration is required when initiating treatment. Doses should be adjusted according to individual response.

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 minimally effective dose.

Predominant negative symptoms (deficit syndrome)

A daily dose between 50 mg and 300 mg is recommended. Doses should be adjusted individually.

Amisulpride can be administered once daily at doses up to 300 mg, higher doses should be administered twice daily.

The minimum effective dose should be used.

Special populations

Elderly patients over 65 years

Treatment of elderly patients is not recommended. The safety of amisulpride has been examined in a limited number of elderly patients. If treatment with amisulpride is absolutely necessary, particular caution is required due to a possible risk of hypotension or sedation. Reduction in dosage may also be required because of renal insufficiency.

Paediatric population

The efficacy and safety of amisulpride in children and adolescents under 18 years of age have not been established. There are only limited data available on the use of amisulpride in adolescents in schizophrenia. Therefore, amisulpride should not be used in adolescents from 15 to 18 years of age until further data are available. If absolutely required, treatment of adolescents must be initiated and performed by a physician experienced in treating

schizophrenia in this age group. The use of amisulpride is contraindicated in children and adolescents under 15 years of age

Renal insufficiency

Amisulpride is eliminated by the 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), amisulpride should not be used in these patients (see section 4.4).

Hepatic insufficiency

Since amisulpride is weakly metabolised, a dosage reduction should not be necessary.

Method of administration

For oral use.

Tablets should be swallowed whole or halved, with a sufficient amount of liquid. Amisulpride can be administered independently from meals.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed
- Concomitant prolactin-dependent tumours e.g. pituitary gland prolactinomas or breast cancer.
- Phaeochromocytoma.
- Children and adolescents under 15 years of age Lactation
- In combination with levodopa

4.4 Special warnings and precautions for use

As with other neuroleptics, Neuroleptic Malignant Syndrome, a potentially fatal complication, characterised by hyperthermia, muscle rigidity and autonomic instability, and elevated CPK may occur. In the event of hyperthermia, particularly with high daily doses, all antipsychotic drugs including amisulpride should be discontinued.

As with other ant dopaminergic agents, caution should be also exercised when prescribing amisulpride to patients with Parkinson's disease, since it may cause worsening of the disease. Amisulpride should be used only if neuroleptic treatment cannot be avoided.

Prolongation of the QT interval:

Amisulpride induces a dose-dependent prolongation of the QT interval (see section 4.8). This effect is known to potentiate the risk of serious ventricular arrhythmias such as torsade dePointes. 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 medicinal product likely to produce pronounced bradycardia (<

55 bpm), hypokalaemia, decreased intracardiac conduction, or prolongation of the QT interval.

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 amisulpride should be reduced if QT is prolonged and discontinued if QTc is >500ms.

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

Concomitant use with antipsychotics should be avoided

***Stroke*:**

In randomised clinical trials versus placebo performed in a population of elderly patients with dementia and treated with certain atypical antipsychotic drugs, 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 drugs, or other populations of patients cannot be excluded. Amisulpride should be used with caution in patients with stroke risk factors.

Elderly patients with dementia:

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug- treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. 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 drugs, treatment with conventional antipsychotic drugs may increase mortality.

The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear.

Venous thromboembolism:

Cases of venous thromboembolism, (VTE) have been reported with antipsychotic drugs. 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 Amisulpride and preventative measures undertaken.

***Breast cancer*:** Amisulpride 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 amisulpride therapy.

Benign pituitary tumour:

Amisulpride may increase prolactin levels. Cases of benign pituitary tumours such as

prolactinoma have been observed during amisulpride therapy (see section 4.8). In case of very high levels of prolactin or clinical signs of pituitary tumour (such as visual field defect and headache), pituitary imaging should be performed. If the diagnosis of pituitary tumour is confirmed, the treatment with amisulpride must be stopped

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

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

4.5 Drugs interactions

Contraindicated combinations

- Levodopa: reciprocal antagonism of effects between levodopa and neuroleptics. Amisulpride may oppose the effect of dopamine agonists e.g. Bromocriptine, ropinirole.

Combinations not recommended

AMAZEO may enhance the central effects of alcohol.

Combinations to be taken into account

- CNS depressants including narcotics, anaesthetics, analgesics, sedative H1 antihistamines, barbiturates, benzodiazepines and other anxiolytic drugs, clonidine and derivatives
- Antihypertensive drugs and other hypotensive medications
- Co-administration of amisulpride and clozapine may lead to an increase in plasma levels of amisulpride
- Caution is advised when prescribing amisulpride with medicines known to prolong the QT interval, e.g., class IA antiarrythmics (e.g., quinidine, disopyramide) and class III antiarrhythmics (e.g. amiodarone, sotalol), some antihistaminic, some other antipsychotics and antimalarial (e.g., mefloquine) (see Section 4.4).

4.6 Pregnancy and lactation

Pregnancy

In animals, amisulpride did not show reproductive toxicity. A decrease in fertility linked to the pharmacological effects of the drug (prolactin mediated effect) was observed. No teratogenic effects of amisulpride were noted.

Very limited clinical data on exposed pregnancies are available. Therefore, the safety of amisulpride during human pregnancy has not been established. Use of the drug is not recommended during pregnancy unless the benefits justify the potential risks.

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

Neonates exposed to antipsychotics, including amisulpride, 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.

Breast-feeding

Amisulpride is excreted into breastmilk in rather large amounts above the accepted value of 10% of the maternal weight-adjusted dosage in some cases, but blood concentrations in breastfed infants have not been evaluated. There is insufficient information on the effects of amisulpride in newborns/infants. A decision must be made whether to discontinue breast-feeding or to abstain from amisulpride therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Fertility

A decrease in fertility linked to the pharmacological effects of the drug (prolactin-mediated effect) was observed in treated animals.

4.7 Effects on ability to drive and use machines

Even when used as recommended, amisulpride may cause somnolence so that the ability to drive vehicles or operate machinery can be impaired.

4.8 Undesirable effects

Adverse effects have been ranked under headings of frequency using the following convention: very common (≥ 1/10); common (≥ 1/100; < 1/10); uncommon (≥ 1/1,000; < 1/100); rare (≥ 1/10,000; < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

Blood and lymphatic system disorders:

Uncommon: leukopenia, neutropenia

Rare: agranulocytosis

Immune system disorders:

Uncommon: allergic

reaction Endocrine

disorders:

Common: amisulpride causes an increase in plasma prolactin levels which is reversible after drug discontinuation. This may result in galactorrhoea, amenorrhoea, gynaecomastia, breast pain, and erectile dysfunction.

Rare: benign pituitary tumour such as prolactinoma (see sections 4.3 and

4.4) Metabolism and nutrition disorders:

Uncommon: hyperglycaemia (see section 4.4), hypertriglyceridemia and hypercholesterolaemia

Rare: hyponatraemia, syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Psychiatric disorders:

Common: insomnia, anxiety, agitation, orgasmic dysfunction

Uncommon: confusion

Nervous system

disorders:

Very common: extrapyramidal symptoms may occur: tremor, rigidity, hypokinesia, hyper salivation, akathisia, and dyskinesia. These symptoms are generally mild at optimal dosages and partially reversible without discontinuation of amisulpride 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.

Common: somnolence, acute dystonia (spasm torticollis, oculogyric crisis, trismus) may appear. This is reversible without discontinuation of amisulpride upon treatment with an antiparkinsonian agent.

Uncommon: seizures, tardive dyskinesia characterized by rhythmic, involuntary movements primarily of the tongue and/or face have been reported, usually after long term administration. Antiparkinsonian medication is ineffective or may induce aggravation of the symptoms.

Rare: Neuroleptic Malignant Syndrome (see section 4.4), which is a potentially fatal complication

Not known: restless legs syndrome

Eye disorders:

Common: blurred vision

Cardiac disorders:

Uncommon: bradycardia

Rare: QT interval prolongation, ventricular arrhythmias such as torsade de pointes, ventricular tachycardia, ventricular fibrillation, cardiac arrest, sudden death

Vascular disorders:

Common: hypotension

Uncommon: increase in blood pressure

Rare: venous thromboembolism, including pulmonary embolism, sometimes fatal, and deep vein thrombosis

Respiratory, thoracic and mediastinal disorders:

Uncommon: nasal congestion, pneumonia aspiration (mainly in association with other antipsychotics and CNS depressants).

Gastrointestinal disorders

Common: constipation, nausea, vomiting, dry

mouth Hepatobiliary disorders:

Uncommon: hepatocellular injury

Skin and subcutaneous tissue disorders:

Rare: angioedema, urticaria

Not known: photosensitivity reaction

Musculoskeletal and connective tissue disorders:

Uncommon: osteopenia, osteoporosis

Renal and urinary disorders:

Uncommon: urinary retention

Pregnancy, puerperium and perinatal conditions:

Not known: drug withdrawal syndrome neonatal Investigations:

Common: weight gain

Uncommon: elevations of hepatic enzymes, mainly transaminases

4.9 Overdose

Experience with amisulpride in overdosage is limited. Exaggeration of the known pharmacological effects of the drug has been reported. These include drowsiness, sedation, hypotension, extrapyramidal symptoms, and coma. Fatal outcomes have been reported mainly in combination with other psychotropic agents.

In cases of acute overdose, the possibility of multiple drug intake should be considered.

Since amisulpride is weakly dialysed, haemodialysis is of no use to eliminate the drug.

There is no specific antidote to amisulpride. Appropriate supportive measures should therefore be instituted with close supervision of vital functions including continuous cardiac monitoring due to the risk of prolongation of QT interval until the patient recovers.

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

5. Pharmacological properties

5.1 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.

5.2 Pharmacodynamicproperties

Pharmacotherapeutic group: Antipsychotics, ATC code N05A L05

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.

Unlike classical and atypical neuroleptics, amisulpride has no affinity for serotonin, PROPORTIONAL TO (8733)-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 AMAZEO against both negative and positive symptoms of schizophrenia.

5.3 Pharmacokinetic properties

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.

The volume of distribution is 5.8 l/kg, plasma protein binding is low (16%) and no drug interactions are suspected.

Absolute bioavailability is 48%. Amisulpride is weakly metabolized: 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. The elimination half-life of amisulpride is approximately 12 hours after an oral dose.

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.

A carbohydrate rich meal (containing 68% fluids) significantly decreases the AUCs, Tmax and Cmax 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.

Hepatic insufficiency

Since the drug 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 – 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.

Limited pharmacokinetic data in elderly subjects (> 65 years) show that a 10 – 30 % rise occurs in Cmax, T1/2 and AUC after a single oral dose of 50 mg. No data are available after repeat dosing.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

An overall review of the completed safety studies indicates that AMAZEO is devoid of any general, organ-specific, teratogenic, mutagenic or carcinogenic risk. Changes observed in rats and dogs at doses below the maximum tolerated dose are either pharmacological effects or are devoid of major toxicological significance under these conditions. Compared with the

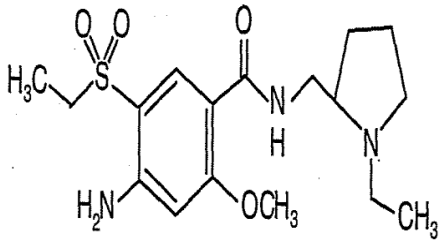
maximum recommended dosages in man, maximum tolerated doses are 2 and 7 times greater in the rat (200 mg/kg/d) and dog (120 mg/kg/d) respectively in terms of AUC. No carcinogenic risk, relevant to man, was identified in the rat at up to 1.5 - 4.5 times the expected human AUC.

A mouse carcinogenicity study (120 mg/kg/d) and reproductive studies (160, 300 and 500 mg/kg/d respectively in rat, rabbit and mouse) were performed. The exposure of the animals to amisulpride during these latter studies was not evaluated.

In animal trials, amisulpride elicited an effect on foetal growth and development at doses corresponding to Human Equivalent Dose of 2000 mg/day and upwards for a 50-kg patient. There was no evidence for a teratogenic potential of amisulpride. Studies on the impact of amisulpride on the behavior of the offspring have not been conducted.

7. .Description

Amazeo 50,100,200,300 Amisulpride is 4-amino-N-[(1-ethyl-2-pyrrolidinyl) methyl]-5-(ethylsulphonyl)-2-methoxybenzamide having molecular formula of C17H27N3O4S and molecular weight is 369.5. The chemical structure is:



Amisulpride is a white or almost white crystalline powder which is freely soluble in dichloromethane, sparingly soluble in ethanol and practically insoluble in water.

Amisulpride Tablets are white to off-white, round, biconvex, film coated tablets plain on both sides. The excipients used are Lactose Monohydrate, Microcrystalline Cellulose, Colloidal Silicon Dioxide, Polyoxyl Stearate, Hydroxy Propyl Methyl Cellulose, Purified Water, Sodium Starch Glycolate, Talc, Magnesium Stearate, Polyethylene Glycol, and Titanium Dioxide.

8. Pharmaceutical particulars

8.1 Incompatibilities

None known.

8.2 Shelf-life

Do not use later than date of expiry

8.3 Packaging information

Amazeo 50,100,200,300 are packed in blister strips of 10 tablets.

8.4 Storage and handing instructions

AMAZEO 50, 100.200 and 300.

Store at a temperature not exceeding 30^0C, protected from light and moisture.Keep the medicines out of reach of children.

9. Patient Counselling Information

AMAZEO

Amisulpride 50 mg, 100 mg, 200 mg tablets Amisulpride 400 mg film-coated tablets Amisulpride

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Read all of this leaflet carefully before you start taking this medicine because it contains Important information for you.

· Keep this leaflet. You may need to read it again.

· If you have any further questions, ask your doctor or pharmacist.

· This medicine has been prescribed for you only. Do not pass it on to others; it may harm Them, even if their signs of illness are the same as yours.

· If you get any side effects, talk to your doctor or pharmacist. This includes any possible side Effects not listed in this leaflet.

What is in this leaflet?

9.1 What AMAZEO is and what it is used for

Amisulpride Tablets contain amisulpride and belongs to a group of medicines called antipsychotics which help to control the symptoms of a mental illness called schizophrenia. Symptoms include:

- Delusions (having strange or unusual thoughts)
- Hallucinations (seeing or hearing things that are not there)
- Being suspicious or aggressive for no apparent reason (these are so called "positive symptoms")
- Becoming withdrawn and subdued (these are so called "negative symptoms").

Amisulpride can be used at the start of and for the long term treatment of schizophrenia.

9.2 What you need to know before you take Amisulpride

Do not take AMAZEO Tablets if:

Are allergic to amisulpride or any of the other ingredients of this medicine (listed in Section 6). Signs of an allergic reaction may include a rash, difficulty swallowing or breathing, swelling of the lips, face, throat or tongue

- Have breast cancer or something called a 'prolactin dependent tumour'.
- Have a tumours on the adrenal gland called phaechromocytoma.
- Are breast-feeding.
- are taking levodopa (used to treat Parkinson's disease) or medicines to treat heart rhythm disorders, or medicines that may cause an abnormal heart rhythm when used at the same time as amisulpride (see "Other medicines and Amisulpride" below)
- Are under 15 years old

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking Amisulpride.

Warnings and precautions

Talk to your doctor or pharmacist before taking your medicine if:

- You have kidney problems
- You have Parkinson's disease
- You have ever had fits (epileptic seizures)
- You are diabetic or have been told you have an increased risk of developing diabetes
- You have an unusual heart rate (rhythm)
- You have heart disease or family history of heart problems or sudden death
- You have a long QT interval or a history of this in the family (this is a measure of the way your heart is working and can be detected by a doctor using an electrocardiogram)
- You had a stroke previously or your doctor has told you that you are at risk of a stroke
- You or someone else in your family has a history of blood clots, as medicines like these have been associated with formation of blood clots
- You or someone else in your family has a history of breast cancer, as amisulpride can affect the risk of developing breast cancer. You should therefore be closely monitored during treatment with Amisulpride
- You have a slow heart beat (less than 55 beats per minute)
- You are taking other medicines that could affect your heart's function: check with your doctor before taking any other medicine. See also under headings "Do not take Amisulpride" and "Other medicines and Amisulpride"
- You have been told you have a low amount of potassium or magnesium in your blood.
- You are elderly. This is because elderly people are more likely to get low blood pressure or feel sleepy. A small increase in the number of deaths of elderly people with dementia has been reported in patients taking antipsychotics compared to those not receiving antipsychotics.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Amisulpride

Other medicines and Amisulpride

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines including medicines obtained without a prescription. This is because amisulpride can affect the way some other medicines work. Also some medicines can affect the way amisulpride works.

In particular, do not take this medicine and tell your doctor if you are taking:

- Bromocriptine or ropinirole (medicines used to treat Parkinson's disease)
- Levodopa, a medicine to treat Parkinson's disease
- Medicines to treat heart rhythm problems (such as quinidine, disopyramide, procainamide, amiodarone, sotalol)
- Cisapride (used to treat stomach problems)
- Bepridil (used to treat angina/chest pain and changes in heart rhythm)
- Sultopride and thioridazine (for schizophrenia)
- Methadone (for pain and drug abuse)
- Halofantrine (to prevent malaria)
- Pentamidine (to treat infections in HIV patients)
- Erythromycin by injection or sparfloxacin (antibiotics)
- Medicines for fungal infections, such as clotrimazole
- Vincamine by injection (used for various brain disorders) Tell your doctor if you are taking any of the following medicines:
- Medicines used to treat high blood pressure or other heart problems that could slow your heart rate down. These include beta-blockers (such as nebivolol or bisoprolol, diltiazem, verapamil, clonidine, guanfacine, digoxin or digoxin-like medicines
- medicines which can cause low potassium levels including diuretics ("water tablets"), some laxatives, amphotericin B (by injection), glucocorticoids (used for conditions such as asthma or rheumatoid arthritis) and tetracosactide (may be used in clinical investigations) • medicines used to treat schizophrenia such as pimozide or haloperidol
- Imipramine or lithium (used to treat depression)
- Some antihistamines such as astemizole and terfenadine (for allergies)
- Other anti-psychotic medicines used for mental health problems
- Medicines for severe pain called opiates such as morphine or pethidine
- Medicines which help you sleep such as barbiturates and benzodiazepines
- Pain-killers such as tramadol and indomethacin

- Anaesthetics
- Antihistamines (for allergies) which make you sleepy, such as promethazine.

Amisulpride with alcohol

Do not drink alcohol while you are taking Amisulpride. This is because Amisulpride can increase the effects of alcohol.

Pregnancy and breast-feeding

Do not take this medicine if you are breast-feeding or planning to breastfeed. If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. The following symptoms may occur in newborn babies of mothers that have used Amisulpride in the last trimester (last three months of pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems and difficulty in feeding. If your baby develops any of these symptoms you may need to contact your doctor.

Driving and using machines

You may feel less alert, drowsy or sleepy while taking this medicine. If this happens, do not drive or use any tools or machines.

Amisulpride tablets contain lactose.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine

9.3 How to take AMAZEO Tablets

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Adults

If you suffer from positive symptoms, the recommended dose is between 400 mg and 800 mg daily, and will be adjusted by your doctor depending on the nature and severity of your illness and your kidney function. The maximum daily dose is 1,200 mg.

If you suffer from both positive and negative symptoms, your doctor will adjust your dose so that there is adequate control of the positive symptoms. To maintain treatment, your doctor will use the lowest possible dose that is effective for you.

If you suffer from mostly negative symptoms, the recommended dose is between 50 mg and 300 mg daily, and will be adjusted by your doctor depending on the nature and severity of your illness and your kidney function.

Patients over 65 years: Amisulpride can cause sedation (drowsiness) or a fall in blood pressure, and is not generally recommended as there is only limited experience in this age group

Use in children and adolescents: Efficacy and safety of amisulpride in children and adolescents under 18 years of age have not been established. If absolutely required, treatment of adolescents from 15 to 18 years of age must be initiated and performed by a physician experienced in treating schizophrenia in this age group. Children and adolescents under 15 years of age must not take these tablets (see section 2 "Do not take Amisulpride").

Patients with kidney problems

Your doctor will normally give you a lower dose. This may be half or a third of the usual daily dose, depending on how well your kidneys are working. How to take this medicine:?

- Swallow the tablets with a glass of water.
- You can take them during or between meals.
- Doses up to 300 mg per day can be taken as a single dose preferably at the same time each day.
- Doses above 300 mg should be taken as half in the morning and half in the evening.
- The 100 mg, 200 mg and 400 mg tablets can be divided into equal doses.

If you take more Amisulpride than you should Contact your doctor or hospital immediately. Take the tablets, leaflet and/or carton with you so the doctor knows what you have taken. The following effects may happen: feeling restless or shaky, rigid muscles, low blood pressure, feeling drowsy or sleepy which could lead to a loss of consciousness.

If you forget to take Amisulpride take it as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose. Do not take a double dose to make up for a forgotten dose. If you stop taking Amisulpride Keep taking your tablets until your doctor tells you to stop. Do not stop taking them just because you feel better.

If you stop, your illness may get worse or come back. Unless your doctor tells you to, stopping treatment suddenly may cause withdrawal effects such as feeling sick, vomiting, sweating, difficulty sleeping, extreme restlessness, muscle stiffness or abnormal movements, or your original condition may come back. To avoid such effects it is important to reduce the dose gradually according to your doctor's instructions.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Stop taking Amisulpride and see a doctor or go to a hospital immediately if you notice any of the Following side effects:

Uncommon (may affect up to 1 in 100 people)

A serious allergic reaction. The signs may include an itchy, lumpy rash, difficulty swallowing or Breathing, swelling of your lips, face, throat or tongue

A fit (seizure)

Not known (frequency cannot be estimated from the available data)

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 in breathing. If you notice any of these signs, seek medical advice immediately.

You get more infections than usual, causing fever, sore throat or mouth ulcers. This could be because of a decrease in the number, or lack of white blood cells.

Tell your doctor as soon as possible if you have any of the following side effects: Very

common (may affect more than 1 in 10 people)

Common (may affect up to 1 in 10 people)

- Movements that you cannot control, mainly of the head, neck, jaw or eyes.

Uncommon (may affect up to 1 in 100 people)

- Movements that you cannot control, mainly of the face or tongue

Other side effects include:

Common (may affect up to 1 in 10 people)

- Difficulty sleeping (insomnia) or feeling anxious or
- agitated Feeling drowsy or sleepy
- Constipation, feeling or being sick, dry
- mouth Putting on weight
- Low blood pressure, which may cause you to feel dizzy
- Increased blood levels of prolactin (a protein), which would be seen in a test and may cause:
- Breast pain or enlargement, unusual production of breast milk (these can occur in women and Men)
- Menstrual problems such as missed periods
- Sexual effects such as problems reaching orgasm or difficulty in getting or maintaining an Erection
- Unusual growth in the pituitary gland

Uncommon (may affect up to 1 in 100 people)

- Slowing of the heart beat
- High blood sugar (hyperglycaemia)
- Increase in liver enzymes, which would be seen in a blood

test Rare (may affect up to 1 in 1,000 people)

- Withdrawal symptoms after stopping treatment of high doses of amisulpride. These may include Feeling or being sick difficulty sleeping, extreme restlessness, muscle stiffness or abnormal Movements, or your original illness may come back.

Not known (frequency cannot be estimated from the available data)

- Withdrawal symptoms seen in newborn babies where the mother has taken this medicine.
- Raised levels of certain fats (triglycerides) and cholesterol in the blood
- Confusion
- Low levels of sodium in your blood which may be seen in blood tests (hyponatraemia).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any

possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store AMAZEO Tablets.

Store at a temperature not exceeding 30ºC, protected from light and moisture.Keep the medicines out of reach of children.

9.6 Content of the pack and other information

Amazeo 50,100,200,300

Amisulpride I.P, 50 mg, Amisulpride I.P.100 mg, Amisulpride I.P. 200 mg, Amisulpride I.P. 300 mg

The excipients used are Lactose Monohydrate, Microcrystalline Cellulose, Colloidal Silicon Dioxide, Polyoxyl Stearate, Hydroxy Propyl Methyl Cellulose, Purified Water, Sodium Starch Glycolate, Talc, Magnesium Stearate, Polyethylene Glycol, and Titanium Dioxide.

10. Details of manufacturer

AMAZEO 50

Ravenbhel Biotech,

EPIP, SIDCO, Kartholi, Bari-

Brahmana, Jammu-181133.

AMAZEO 100, 200

Torrent Pharmaceuticals

Ltd 32 No. Middle

Camp, NH-10 East

District, Gangtok, Sikkim

737 135

OR

Biodeal Pharmaceuticals Pvt. Ltd.

Vill. Sainimajra, Nalagarh-Ropar Road,

Nalagarh, Distt. Solan (H.P.)

AMAZEO 300

Torrent Pharmaceuticals Ltd

Vill. Bhud & Makhnu Majara, Teh. Baddi- 173205

Dist.Solan (H.P.), INDIA.

11. Details of permission or licence number with date

AMAZEO 50

JK/01/11-12/192 issued on 04.09.2015

AMAZEO 100, 200

MNB/05/183 issued on 26.10.2017

OR

MNB/06/440 issued on 10.11.2020

AMAZEO 300

MNB/05/183 issued on 09.12.2020

12. Date of revision

Oct 2019

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

Indrad-382 721, Dist. Mehsana, INDIA.

IN/ AMAZEO 50,100,200,300 mg Tablets /Oct-22/03/PI