SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

< Invented name> 50 mg Tablets
< Invented name> 100 mg Tablets
< Invented name> 200 mg Tablets
< Invented name> 400 mg Film-coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg amisulpride
Each tablet contains 100 mg amisulpride
Each tablet contains 200 mg amisulpride
Each tablet contains 400 mg amisulpride

Excipient with known effect:
50 mg tablet: Each tablet contains 16.28 mg lactose monohydrate
100 mg tablet: Each tablet contains 32.56 mg lactose monohydrate
200 mg tablet: Each tablet contains 65.12 mg lactose monohydrate
400 mg tablet: Each tablet contains 130.25 mg lactose monohydrate

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet (50 mg, 100 mg, 200 mg)
Film-coated tablet (400 mg)

50mg: White round tablet with 'AA 50' on one side and 'G' on the reverse, 6 mm in diameter.
100 mg: White round tablet with 'AMI' breakline '100' on one side and 'G' on the reverse, 7.5 mm in diameter.
200 mg: White round tablet with 'AMI' breakline '200' on one side and 'G' on the reverse, 10 mm in diameter.
400 mg: White film coated, capsule shaped tablet, embossed with "AS 400" on one side and a break-line on the reverse, ~~dimensions~~ 18mm ~~x 7.7mm~~in length.

100 mg, 200 mg, 400 mg: The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<Invented name> is indicated for the treatment of acute and chronic schizophrenic disorders with:

- positive symptoms (such as delusions, hallucinations, thought disorders, hostility, suspiciousness), and/or
- negative symptoms (deficit syndrome) such as blunted affect, emotional and social withdrawal

This includes patients with predominant negative symptoms.

4.2 Posology and method of administration

Posology

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.

< Invented name> 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 (see section 4.3).

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.

Duration of treatment
Data from controlled clinical trials covering a period of 1 year is available. The duration of treatment should be determined by the treating physician.

To avoid withdrawal symptoms treatment should be discontinued gradually (see section 4.4).

For doses not practicable with this strength, other strengths of this medicinal product are available.

Method of administration
For oral use.
Tablets should be swallowed whole or halved, with a sufficient amount of liquid.
<Invented name> can be administered independently from meals.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Concomitant prolactin-dependent tumours e.g. pituitary gland prolactinomas or breast cancer.
- Phaeochromocytoma.
- Children and adolescents under 15 years of age (see section 4.2).
- In combination with levodopa (see section 4.5).
- In combination with the following medicinal products which could induce torsade de pointes (see section 4.5):
    - class Ia antiarrhythmics such as quinidine and disopyramide
    - class III antiarrhythmics such as amiodarone and sotalol
    - other medicinal products such as bepridil, cisapride, sultopride, thioridazine, methadone, erythromycin (intravenous application), vincamine (intravenous application), halofantrine, pentamidine, sparfloxacin, azole antifungals

4.4 Special warnings and precautions for use

Severe liver toxicity has been reported with amisulpride use. Patients should be instructed to immediately report signs such as asthenia, anorexia, nausea, vomiting, abdominal pain or icterus to a physician. Investigations including clinical examination and biological assessment of liver function should be undertaken immediately (see section 4.8).

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 antidopaminergic 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 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 medicinal product 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 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 (see section 4.5).

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 <Invented name> 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.

Hyperglycaemia has been reported in patients treated with some atypical antipsychotic agents, including amisulpride, therefore patients with an established diagnosis of diabetes mellitus or with risk factors for diabetes who are started on amisulpride, should get appropriate glycaemic monitoring.

Amisulpride may lower the seizure threshold. Therefore patients with a history of epilepsy should be closely monitored during amisulpride therapy.

Amisulpride 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).

In elderly patients, amisulpride, like other neuroleptics, should be used with particular caution because of a possible risk of hypotension and sedation. Reduction in dosage may also be required because of renal insufficiency.

Withdrawal symptoms, including nausea, vomiting and insomnia, have been described after abrupt cessation of high therapeutic doses of antipsychotic drugs. Recurrence of psychotic symptoms may also occur, and the emergence of involuntary movement disorders (such as akathisia, dystonia, and dyskinesia) has been reported with amisulpride. Therefore, gradual withdrawal of amisulpride is advisable.

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

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 (see section 4.3).

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

4.5 Interaction with other medicinal products and other forms of interaction

Contraindicated combinations (see also section 4.3):
- Medicinal products which could induce torsade de pointes:
  - class Ia antiarrhythmics such as quinidine and disopyramide
  - class III antiarrhythmics such as amiodarone and sotalol
  - other medicinal products such as bepridil, cisapride, sultopride, thioridazine, methadone, erythromycin (intravenous application), vincamine (intravenous application), halofantrine, pentamidine, sparfloxacin, azole antifungals.
- Levodopa: reciprocal antagonism of effects between levodopa and neuroleptics. Amisulpride may oppose the effect of dopamine agonists e.g. bromocriptine, ropinirole.

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

Combinations which require precautions for use:
Concomitant use of the following agents can lead to potentiation of the effect:
- CNS depressants including narcotics, anaesthetics, analgesics, sedative H_1 antihistamines, barbiturates, benzodiazepines and other anxiolytics, 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

4.6 Fertility, pregnancy and lactation

Pregnancy

There is only limited amount of data from the use of amisulpride in pregnant women. . The safety of amisulpride during pregnancy has not been established.
The use of amisulprideis not recommended during pregnancy and in women of child bearing potential not using effective contraception unless the benefits justify the potential risks.

Amisulpride crosses the placenta.

Studies in animals have shown reproductive toxicity (see section 5.3).

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 in breast milk 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 medicinal product (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 and blurred vision and, therefore so that the ability to drive vehicles or operate machinery may be impaired (see section 4.8).

4.8 Undesirable effects

Adverse reactions have been ranked under headings of frequency using the following convention:
Very common (≥1/10);
Common (≥1/100 to <1/10);
Uncommon (≥1/1,000 to <1/100);
Rare (≥1/10,000 to <1/1,000);
Very rare (<1/10,000);
Not known (cannot be estimated from the available data).

System Organ Class	**Frequency**	**Adverse Drug Reaction**
Blood and Lymphatic system disorders	Uncommon	Leukopenia, neutropenia (see section 4.4)
	Rare	Agranulocytosis (see section 4.4)
Immune system disorders	Uncommon	Allergic reactions
Endocrine disorders	Common	Increase in plasma prolactin levels which is reversible after discontinuation of amisulpride. *This may result in:* – galactorrhoea, – amenorrhoea or menstrual disorders, – gynaecomastia, – breast pain or enlargement, – erectile dysfunction.

	Rare	Benign pituitary tumour such as prolactinoma (see sections 4.3 and section 4.4).
Metabolism and nutrition disorders	Uncommon	Hyperglycaemia (see section 4.4), hypertriglyceridaemia 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[1] may occur: – tremor, – rigidity, – hypokinesia, – hypersalivation, – akathisia, – dyskinesia.
	Common	Acute dystonia (spasm torticollis, oculogyric crisis, trismus) may appear.[2] Somnolence.
	Uncommon	Tardive dyskinesia characterised by rhythmic, involuntary movements primarily of the tongue and/or face has been reported, usually after long-term administration.[3] Seizures.
	Rare	Neuroleptic malignant syndrome symptom (see section 4.4), which is a potentially fatal complication.
	Not known	Restless leg syndrome
Eye disorders	Common	Blurred vision (see section 4.7)
Cardiac disorders	Uncommon	Bradycardia.
	Rare	QT interval prolongation. 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	Common	Hypotension.
	Uncommon	Increase in blood pressure
	Rare	Venous thromboembolism, including pulmonary embolism, sometimes fatal, and deep vein thrombosis (see section 4.4).
Respiratory, thoracic and mediastinal disorders	Uncommon	Nasal congestion Aspiration pneumonia (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	Not known	Drug withdrawal syndrome neonatal (see section 4.6)

perinatal conditions		
Investigations	Common	Weight gain
	Uncommon	Elevations of hepatic enzymes, mainly transaminases

[1] 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 50-300mg/day.
[2] This is reversible without discontinuation of amisulpride upon administration of antiparkinsonian medication.
[3] Antiparkinsonian medication should not be used as it is ineffective and may induce aggravation of the symptoms.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system <To be completed nationally>.

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 Pharmacodynamic properties

Pharmacotherapeutic group: Psycholeptics, antipsychotics
ATC code: N05AL05

Amisulpride binds selectively with a high affinity to human dopaminergic D_2/D_3 receptor subtypes whereas it is devoid of affinity for D_1, D_4 and D_5 receptor subtypes.

Unlike classical and atypical neuroleptics, amisulpride has no affinity for serotonin, alpha-adrenergic, histamine H_1 and cholinergic receptors. In addition, amisulpride does not bind to sigma receptors.

In animal studies, at high doses, amisulpride blocks dopamine receptors in the limbic structure in preference to those in the striatum. At low doses it preferentially blocks pre-synaptic D_2/D_3 receptors, producing dopamine release responsible for its disinhibitory effects.

This pharmacological profile explains the clinical efficacy of amisulpride when used for 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%) and no drug interactions are known.

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

Elimination
The elimination half-life of amisulpride is approximately 12 hours after an oral dose. Amisulpride is eliminated unchanged in the urine. 50% 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.

Hepatic impairment:
Since amisulpride is weakly metabolised, a dosage reduction should not be necessary in patients with hepatic insufficiency.

Renal impairment:
The elimination half-life is increased 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.

Older people
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 are 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. 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 to 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 has an effect on fetal growth and development at doses that correspond to Human Equivalent Dose of 2000 mg/day and upwards for a 50 kg patient. No evidence for a

teratogenic potential of amisulpride has been observed. Studies on the impact of amisulpride on the behaviour of the offspring have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Cellulose microcrystalline
Sodium starch glycolate (Type A)
Hypromellose
Magnesium stearate

(400 mg only)
The film-coating contains:
Hypromellose
Titanium dioxide (E171)
Macrogol 400

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions

6.5 Nature and contents of container

PVC/Aluminium foil blister packs containing:
12 tablets (50mg)
20 tablets (50mg, 100mg, 200mg, 400mg)
30 tablets (50mg, 100mg, 200mg, 400mg)
30x1 tablets (100mg, 400mg)
50 tablets (50mg, 100mg, 200mg, 400mg)
60 tablets (50mg, 100mg, 200mg, 400mg)
60x1 tablets (100mg, 200mg)
90 tablets (50mg, 100mg, 200mg, 400mg)
100 tablets (50mg, 100mg, 200mg, 400mg)
120 tablets (200mg)
150 tablets (200mg)
150 (3 cartons of 50) tablets (200 mg)

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

8. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<[To be completed nationally]>

10. DATE OF REVISION OF THE TEXT

<[To be completed nationally]>

LABELLING

.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

< Invented name> 50 mg, 100 mg, 200 mg Tablets
< Invented name> 400 mg Film-coated Tablets

amisulpride

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 50 mg, 100 mg, 200 mg amisulpride.
Each film-coated tablet contains 400 mg amisulpride.

3. LIST OF EXCIPIENTS

Also contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Tablet (50 mg, 100 mg, 200 mg)
Film-coated tablet (400 mg)

12 tablets (50mg)
20 tablets (50mg, 100mg, 200mg, 400mg)
30 tablets (50mg, 100mg, 200mg, 400mg)
30x1 tablets (100mg, 400mg)
50 tablets (50mg, 100mg, 200mg, 400mg)
60 tablets (50mg, 100mg, 200mg, 400mg)
60x1 tablets (100mg, 200mg)
90 tablets (50mg, 100mg, 200mg, 400mg)
100 tablets (50mg, 100mg, 200mg, 400mg)
120 tablets (200mg)
150 tablets (200mg)

5. METHOD AND ROUTE OF ADMINISTRATION

For oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

<invented name> 50 mg, 100 mg, 200 mg tablets
<invented name> 400 mg film-coated tablets

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK

1. NAME OF THE MEDICINAL PRODUCT

< Invented name> 200 mg Tablets

amisulpride

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 200 mg amisulpride.

3. LIST OF EXCIPIENTS

Also contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Tablet.
Multipack: 150 (3 cartons of 50) tablets (200mg).

5. METHOD AND ROUTE OF ADMINISTRATION

For oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

<invented name> 200 mg tablets

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON OF MULTIPACK

1. NAME OF THE MEDICINAL PRODUCT

< Invented name> 200 mg Tablets

amisulpride

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 200 mg amisulpride.

3. LIST OF EXCIPIENTS

Also contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Tablet

50 tablets

Component of a multipack, cannot be sold separately.

5. METHOD AND ROUTE OF ADMINISTRATION

For oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

<invented name> 200 mg tablets

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

PVC/AL BLISTER

1. NAME OF THE MEDICINAL PRODUCT

< Invented name> 50 mg, 100 mg, 200 mg Tablets
< Invented name> 400 mg Film-coated Tablets

amisulpride

(exception for BE : pharmaceutical form and the statement of the active substance will not be mentioned)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PACKAGE LEAFLET

Package leaflet: Information for the patient

<Invented name> 50 mg, 100 mg, 200 mg Tablets
<Invented name> 400 mg film-coated Tablets
amisulpride

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. See section 4.

What is in this leaflet

1. What <Invented name> is and what it is used for

<Invented name> contains 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").

<Invented name> can be used at the start of and for the long term treatment of schizophrenia.

2. What you need to know before you take <Invented name>

Do not take <Invented name> if you:
- 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 tumour on the adrenal gland called phaechromocytoma.
- 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 <Invented name>" 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 <Invented name>.

Warnings and precautions

Severe liver problems have been reported with <Invented name>. Talk to your doctor immediately if you experience fatigue, loss of appetite, nausea, vomiting, abdominal pain or yellow discoloration of the eyes or skin.

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 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 <Invented name>
- 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 <Invented name>" and "Other medicines and <Invented name>"
- 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 <Invented name>.

Other medicines and <Invented name>
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 or 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 bisopralol), 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, clozapine or haloperidol
- imipramine or lithium (used to treat depression)
- some antihistamines such as astemizole and terfenadine (for allergies)
- mefloquine used to treat malaria
- 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

<Invented name> with alcohol
Do not drink alcohol while you are taking <Invented name>. This is because <Invented name> can increase the effects of alcohol.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Pregnancy
<Invented name> is not recommended during pregnancy and in women of childbearing potential not using effective contraception. The following symptoms may occur in newborn babies of mothers that have used <Invented name> in the last trimester (last three months of pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems and difficulty in feeding. If you baby develops any of these symptoms you may need to contact your doctor.

Breast-feeding
You should not breast-feed during therapy with <Invented name>. Talk to your doctor about the best way to feed your baby if you are taking <Invented name>.

Driving and using machines
You may feel less alert, drowsy, sleepy and have blurred vision while taking this medicine.
If this happens, do not drive or use any tools or machines.

<Invented name> **contains lactose**. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take <Invented name>

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 doctor 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 <Invented name>").

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 <Invented name> 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 <Invented name>
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 tablet.

If you stop taking <Invented name>
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.

4. Possible side effects

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

Contact 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)
- 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.

Rare (may affect up to 1 in 1,000 people)
- High temperature, sweating, stiff muscles, fast heartbeat, fast breathing and feel confused, drowsy or agitated. These could be the symptoms of a serious but rare side effect called 'neuroleptic malignant syndrome'
- An unusual heart rate, very fast heart rate or chest pain which could result in a heart attack or life-threatening heart disorder.
- 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.Benign (non-cancerous) pituitary tumour such as prolactinoma.
- Feeling unwell, confused or weak, feeling sick (nausea), loss of appetite, feeling irritable. This could be signs of an illness called syndrome of inappropriate antidiuretic hormone secretion (SIADH).

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)
- Trembling, muscle stiffness or spasm, slow movement, producing more saliva than usual or feeling restless.

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
- Osteoporosis (condition, when your bones are more likely to break) or osteopenia (bone weakening)
- Aspiration pneumonia (a type of lung infection that occurs when food, saliva, liquids, or vomit is breathed into the lungs or airways leading to the lungs, instead of being swallowed into the esophagus and stomach.

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
- Difficulty reaching orgasm
- Blurred vision.
- 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.
  - Difficulty in getting or maintaining an erection.

Uncommon (may affect up to 1 in 100 people)
- Slowing of the heart beat.
- High blood sugar (hyperglycaemia).
- Raised levels of certain fats (triglycerides) and cholesterol in the blood.
- Increase in liver enzymes, which would be seen in a blood test.
- Confusion.
- Increase in blood pressure
- Stuffy nose.
- Urinary retention (if you are not able to completely empty your bladder)
- Liver tissue damage

Rare (may affect up to 1 in 1,000 people)
- Low levels of sodium in your blood which may be seen in blood tests (hyponatraemia).

Not known (frequency cannot be estimated from the available data)
- Restless legs syndrome (uncomfortable feeling in legs temporarily relieved by movement and symptoms getting worse at the end of the day).
- Increased sensitivity of your skin to sun and ultraviolet light.
- Withdrawal symptoms seen in newborn babies where the mother has taken this medicine.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [To be completed nationally]. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store <Invented name>.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and blister after 'EXP'. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What <Invented name>. contains
The active substance is amisulpride.
Each 50 mg tablet contains 50 mg amisulpride.
Each 100 mg tablet contains 100 mg amisulpride.
Each 200 mg tablet contains 200 mg amisulpride.
Each 400 mg tablet contains 400 mg amisulpride.

The other ingredients are lactose monohydrate (see section 2, '<Invented name> contains lactose'), microcrystalline cellulose, sodium starch glycolate (Type A), hypromellose, magnesium stearate.

The film-coating contains hypromellose, titanium dioxide (E171), macrogol 400 (400 mg only).

What <Invented name> looks like and contents of the pack
50mg: White round tablet with 'AA 50' on one side and 'G' on the reverse, 6 mm in diameter.

100 mg: White round tablet with 'AMI' breakline '100' on one side and 'G' on the reverse, 7.5 mm in diameter.
200 mg: White round tablet with 'AMI' breakline '200' on one side and 'G' on the reverse, 10 mm in diameter.
400 mg: White film coated, capsule shaped tablet, embossed with "AS 400" on one side and a break-line on the reverse, ~~dimensions~~ 18mm ~~x 7.7 mm~~in length.

<Invented name> is available in:
Blister packs containing:
12 tablets (50mg)
20 tablets (50mg, 100mg, 200mg, 400mg)
30 tablets (50mg, 100mg, 200mg, 400mg)
30x1 tablets (100mg, 400mg)
50 tablets (50mg, 100mg, 200mg, 400mg)
60 tablets (50mg, 100mg, 200mg, 400mg)
60x1 tablets (100mg, 200mg)
90 tablets (50mg, 100mg, 200mg, 400mg)
100 tablets (50mg, 100mg, 200mg, 400mg)
120 tablets (200mg)
150 tablets (200mg)
150 (3 cartons of 50) tablets (200 mg)

Not all pack sizes may be marketed.

Marketing Authorisation Holder
<[To be completed nationally]>

Manufacturer
McDermott Laboratories Ltd trading as Gerard Laboratories, 36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland
Or
Mylan Hungary Kft./Mylan Hungary Ltd., Mylan utca 1., Komárom, 2900, Hungary

This medicinal product is authorised in the Member States of the EEA under the following names:

<{Name of the Member State}> <{Name of the medicinal product}>

This leaflet was last revised in