**UKPAR Amisulpride 50, 100, 200 and 400mg Tablets**

**AMISULPRIDE 50MG TABLETS**
PL 20176/0010

**AMISULPRIDE 100MG TABLETS**
PL 20176/0011

**AMISULPRIDE 200MG TABLETS**
PL 20176/0012

**AMISULPRIDE 400MG TABLETS**
PL 20176/0013

**UKPAR**

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LAY SUMMARY

The MHRA today granted Technopharm Limited (licences) for the medicinal products Amisulpride 50mg, 100mg, 200mg and 400mg Tablets (PL 20176/0010-3). These are prescription only medicines (POM) for the treatment of acute and chronic schizophrenic disorders, in which positive symptoms (such as delusions, hallucinations, thought disorders) and/or negative symptoms (such as blunted affect, emotional and social withdrawal) are prominent, including patients characterised by predominant negative symptoms.

Amisulpride 50mg, 100mg, 200mg and 400mg Tablets contain the active ingredient amisulpride, which binds selectively with a high affinity to human dopaminergic D₂/D₃ receptor subtypes.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Amisulpride 50mg, 100mg, 200mg and 400mg Tablets outweigh the risks, hence Marketing Authorisations have been granted.
SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal products Amisulpride 50mg, 100mg, 200mg and 400mg to Technopharm Limited (PL 20176/0010-13) on 6th June 2006. The products are prescription only medicines.

The applications were submitted as abridged applications according to Article 10.1 of Directive 2001/83/EC, as amended, claiming essential similarity to the original products Solian 50mg, 100mg, 200mg and 400mg Tablets (Sanofi-Synthelabo) which have been authorised in the EU for more than 10 years.

The products contain the active ingredient amisulpride and are indicated for the treatment of acute and chronic schizophrenic disorders, in which positive symptoms (such as delusions, hallucinations, thought disorders) and/or negative symptoms (such as blunted affect, emotional and social withdrawal) are prominent, including patients characterised by predominant negative symptoms.

Amisulpride binds selectively with a high affinity to human dopaminergic D₂/D₃ receptor subtypes. It no affinity for D₁, D₄ and D₅ receptor subtypes or serotonin, α-adrenergic, histamine H₁ and cholinergic receptors.
PHARMACEUTICAL ASSESSMENT

Active substance
INN: Amisulpride
Chemical Name: 4 amino-N-[(2RS)-1-ethylpyrrolidin-2-yl]methyl]-5-(ethylsulphonyl)-2-methoxybenzamide (as stated in Ph.Eur)
4-amino-N-[(1ethyl-2-pirrolidinylmethyl]-5-(ethylsulfonyl)-o-anisamide
Molecular Formula: C₁₇H₂₇N₃O₄S
Molecular Weight: 369.5
Appearance: White or almost white, crystaline powder, bitter taste

Synthesis of the drug substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

An appropriate specification is provided for the active substance lansoprazole.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Appropriate proof of structure has been supplied for the active pharmaceutical ingredient.

All potential known impurities have been identified and characterised.

Batch analysis data are provided and comply with the proposed specification.

Appropriate stability data have been generated showing amisulpride to be a physically and chemically stable drug. The data support a shelf life of 3 years.

Other ingredients
Other ingredients consist of maize starch, lactose monohydrate, methylcellulose 400cp, colloidal silica anhydrous, magnesium stearate and purified water in the 50mg, 100mg and 200mg Tablets. Other ingredients consist of lactose monohydrate, methylcellulose 400cp, sodium starch glycollate, magnesium stearate, microcrystalline cellulose, purified water, film coating (methacrylate polymers and eudragit E100), titanium dioxide, talc, macrogol 6000, and isopropyl alcohol and purified water as solvents (which are removed during drying) for the 400mg Tablets.

With the exception of Eudragit E100, all excipients comply with their respective Ph Eur monographs. Eudragit E100 is a mixture of cationic copolymer based on dimethylaminoethylmethacrylate and neutral methacrylic esters. A satisfactory specification has been provided.
Satisfactory certificates of analysis have been provided for all ingredients showing compliance with their respective monograph/specifications.

Lactose monohydrate and magnesium stearate are the only ingredients that come from animal sources. The lactose used to produce lactose monohydrate is sourced from healthy animals under the same conditions as milk for human consumption. A satisfactory certificate of suitability has been provided for the stearic acid used to make magnesium stearate. The producer of magnesium stearate has further stated that all future batches will be of vegetable origin.

All strengths of tablet are packaged in aluminium/PVC blister strips. Pack sizes for all strengths are 60 tablets. Satisfactory specifications and certificates of analysis have been provided for the packaging components. It is confirmed that the PVC conforms with food Directive 90/128/EC. It is stated that the aluminium complies with rule CEN EN 602:1994 – aluminium and aluminium alloys – wrought products – chemical composition of semi products used for the fabrication of articles for use in contact with food. The resins lacquered onto the aluminium have been shown to comply with relevant guidelines related to contact with foodstuffs.

**Product development and finished product specification**

The rationale for the type of pharmaceutical form developed and formulation variables evaluated during development have been stated and are satisfactory.

The rationale and function of each excipient added is discussed. Levels of each ingredient are typical for a product of this nature and have been optimised on the basis of results from development studies.

Comparative *in vitro* dissolution profiles have been generated for the proposed and reference products with satisfactory results. Comparative impurity studies have also been undertaken.

Satisfactory batch formulae have been provided for the manufacture of the product along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results at pilot-scale. Additionally, a commitment has been provided that the first full-scale commercial production batches will be validated.

The finished product specifications proposed for both release and shelf life are acceptable and provide an assurance of the quality and consistency of the finished products. The analytical methods used have been suitably validated. Batch analysis data has demonstrated compliance with the proposed release specifications.

**Stability of the product**

All results from stability studies on pilot batches were within specified limits. These data support a shelf-life of 24 months, with storage conditions ‘Do not store above 25°C.’

**Bioequivalence/bioavailability**

Satisfactory Certificates of Analysis have been provided for the test and reference batches.
SPC, PIL, Labels
The SPC, PIL and Labels are pharmaceutically acceptable.

CONCLUSION
It is recommended that Marketing Authorisations are granted for these applications.

The requirements for essential similarity of the proposed and reference products have been met with respect to qualitative and quantitative content of the active substance. In addition, similar dissolution profiles have been demonstrated for the proposed and reference products.
PRECLINICAL ASSESSMENT

These applications for generic products claims essential similarity to Solian 50mg, 100mg, 200mg and 400mg Tablets (Sanofi-Synthelabo), which have been licensed within the EEA for over 10 years.

No new preclinical data have been supplied with these applications and none are required for an application of this type.
CLINICAL ASSESSMENT

1. INTRODUCTION AND BACKGROUND
These are standard abridged national applications for Amisulpride 50mg, 100mg, 200mg and 400mg Tablets submitted under Article 10.1 of Directive 2001/83/EC, as amended. The applications cross-refer to Solian 50mg, 100mg, 200mg and 400mg Tablets (Sanofi-Synthelabo) which have been authorised in the EU for more than 10 years.

2. INDICATIONS
The indications proposed are essentially identical to those of reference product, Solian 50mg, 100mg, 200mg and 400mg (as approved in the UK) and are, therefore, satisfactory.

3. DOSE & DOSE SCHEDULE
The dose and dose schedule are essentially identical to that of the reference product Solian 50mg, 100mg, 200mg and 400mg (as approved in the UK) and are, therefore, satisfactory.

4. CLINICAL PHARMACOLOGY
Amisulpride binds selectively with a high affinity to human dopaminergic D₂/D₃ receptor subtypes. It no affinity for D₁, D₄ and D₅ receptor subtypes or serotonin, α-adrenergic, histamine H₁ and cholinergic receptors.

4.1 Bioequivalence
Two bioequivalence studies are presented. Differences for the 400mg dosage form necessitate an additional study for this strength. The clinical expert does not fully justify the applicability of the bioequivalence study performed on the 200mg strength to the 50mg and 100mg products as only the pharmaceutical proportionality is considered. Nevertheless there are adequate published data to illustrate linearity of kinetics up to 1200mg daily.

Both studies were carried out in accordance with Good Clinical Practice in 2002. The reference product chosen was Solian manufactured by Sanofi Synthelabo in France.

Study FARMOVS 57-2002
In this comparative, randomised, two-way, two-period, single dose crossover study, 41 healthy fasted male volunteers received a single 400mg tablet orally of either the applicant's test product or the reference product Solian. Serum drug levels of amisulpride were followed for 72 hours following dosing and the schedule was appropriate for accurate determination of AUC_{inf} and C_{max}. The washout period of 14 days between phases was sufficiently long. The randomisation scheme was balanced for sequence and appears random.

Log-transformed data for AUC_t, AUC_{inf} and C_{max} were analysed by ANOVA.

Results
There were two premature withdrawals (excluded from the analysis) but no other major protocol violators. There were no sequence or period effects. Bioequivalence results for log-transformed test/reference ratios with 90% Confidence Intervals:
AUC_t  0.994 (0.95 – 1.04)  
AUC_inf  0.994 (0.95 – 1.04)  
C_max  0.920 (0.82 – 1.03)  

T_max was 4. hrs for test product, 4.5 hrs reference

Assessor's Comment  
Bioequivalence for the 400mg product has been satisfactorily demonstrated in accordance with CPMP criteria.

Study FARMOV S 56-2002  
In this comparative, randomised, two-way, two-period, single dose crossover study, 36 healthy fasted male volunteers received a single 200mg tablet orally of either the applicant's test product or the reference product Solian. Serum drug levels of amisulpride were followed for 60 hours following dosing and the schedule was appropriate for accurate determination of AUC_inf and C_max. The washout period of 7 days between phases was sufficiently long. The randomisation scheme was balanced for sequence and appears random.

Log-transformed data for AUC_t, AUC_inf and C_max were analysed by ANOVA.

Results  
One subject withdrew during the study for unrelated reasons. There no other major protocol violators and no sequence or period effects. Bioequivalence results for log-transformed test/reference ratios with 90% Confidence Intervals:

AUC_t  0.978 (0.92 – 1.04)  
AUC_inf  0.987 (0.94 – 1.04)  
C_max  0.991 (0.87 – 1.14)  

T_max was 4. hrs for test product, 3.5 hrs reference

Assessor's Comment  
Bioequivalence has been satisfactorily demonstrated for the 200mg product in accordance with CPMP criteria.

5. EFFICACY  
No new data on the efficacy of amisulpride are submitted and none are required for this type of application.

6. SAFETY  
No new data on the safety of amisulpride are submitted and none are required for this type of application.
7. EXPERT REPORTS
A clinical expert report is provided, written by an appropriately qualified individual. It includes a suitable review of the bioequivalence studies.

8. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
The SPC is essentially identical to the SPC for the reference product Solian approved in the UK and is satisfactory.

9. PATIENT INFORMATION LEAFLET (PIL)
A full colour mock-up is provided and is satisfactory.

10. LABELLING
The labelling is satisfactory.

11. APPLICATION FORM (MAA)
The MAA is satisfactory.

12. DISCUSSION
Bioequivalence has been satisfactorily demonstrated for the 200mg and 400mg products in accordance with CPMP criteria. Satisfactory data have been provided to show linear kinetics between the 50mg, 100mg and 200mg doses, so the claim of bioequivalence is satisfactory for all doses of the applicant’s product.

The SPC and PIL are mostly identical to the SPC for the reference product Solian approved in the UK and is satisfactory.

13. MEDICAL CONCLUSION
Marketing authorisations may be granted for these preparations.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Amisulpride 50mg, 100mg, 200mg and 400mg Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
Bioequivalence has been demonstrated between the applicant’s Amisulpride 200mg Tablets and Solian 200mg Tablets (Sanofi-Synthelabo). Given that linear kinetics apply between the 50mg and 200mg capsules, that proportional formulae for the capsules have been used and that similar dissolution results have been shown for the two strengths, a separate bioequivalence study using the 50mg or 100mg tablets is not considered necessary. A separate bioequivalence study was carried out for the 400mg tablets, and bioequivalence was demonstrated between the applicant’s Amisulpride 400mg Tablets and Solian 400mg Tablets (Sanofi-Synthelabo)

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for Solian Tablets.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant’s products and the innovator products are interchangeable. Extensive clinical experience with amisulpride is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.
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**STEPS TAKEN FOR ASSESSMENT**

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<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 3rd December 2003</td>
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<td>Following assessment of the applications the MHRA requested further information relating to the clinical dossiers on 9th March 2004, and further information relating to the quality dossiers on 2nd March 2004, 4th November 2004.</td>
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<td>The applicant responded to the MHRA’s requests, providing further information on 16th June 2004, and again on 30th December 2004.</td>
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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
   Amisulpride 50 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
   Each tablet contains 50 mg amisulpride.
   For excipients please refer to section 6.1.

3. PHARMACEUTICAL FORM
   Amisulpride tablets 50 mg are white to off white, round tablets with breakline marked with AM with the breakline in the middle (i.e. A/M) on one side and 50 on the other.
   Diameter: 7 mm, diameter 7 mm.

4. CLINICAL PARTICULARS
   4.1. Therapeutic indications
   Treatment of acute and chronic schizophrenic disorders, in which positive symptoms (such as delusions, hallucinations, thought disorders) and/or negative symptoms (such as blunted affect, emotional and social withdrawal) are prominent, including patients characterised by predominant negative symptoms

   4.2. Posology and method of administration
   For acute psychotic episodes, oral doses between 400 mg/d and 800 mg/d are recommended. In individual cases, the daily dose may be increased up to 1200 mg/d. Doses above 1200 mg/d have not been extensively evaluated for safety and therefore should not be used. No specific titration is required when initiating the treatment with amisulpride. 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.

   For patients characterised by predominant negative symptoms, oral doses between 50 mg/d and 300 mg/d are recommended. Doses should be adjusted individually.

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

   Elderly: Amisulpride should be used with particular caution because of a possible risk of hypotension or sedation.

   Children: Amisulpride is contra-indicated in children under 15 years of age as its safety has not yet been established.

   Renal insufficiency: Amisulpride is eliminated by the 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. As there is no experience in patients with severe renal impairment (CRCL < 10 ml/min) particular care is recommended in these patients. (see 4.4 Special warnings and precautions for use)

   Hepatic insufficiency: since the drug is weakly metabolised a dosage reduction should not be necessary.

   4.3. Contraindications
   - Hypersensitivity to the active ingredient or to other ingredients of the drug;
   - Concomitant prolactin-dependent tumours e.g. pituitary gland prolactinomas and breast cancer;
- Phaeochromocytoma;
- Children under 15 years of age;
- Pregnancy or lactation;
- Women of childbearing potential unless using adequate contraception.

Combination with the following medications which could induce torsades de pointes:
- Class Ia antiarrhythmic agents such as quinidine, disopyramide, procainamide;
- Class III antiarrhythmic agents such as amiodarone, sotalol;
- Others medications such as bepridil, cisapride, sulthiame, thioridazine, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin.
This list is not exhaustive.

- Combination with levodopa (see 4.5 Interactions with other medical products and other forms of interaction)

4.4. Special warnings and precautions for use

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

Amisulpride is eliminated by the renal route. In cases of severe renal insufficiency, the dose should be decreased and intermittent treatment should be prescribed (see 4.2 Posology and method of administration).

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

In elderly patients, amisulpride, like other neuroleptics, should be used with particular caution because of a possible risk of hypotension or sedation.

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. This effect, known to potentiate the risk of serious ventricular arrhythmias such as torsades de pointes is enhanced by the pre-existence of bradycardia, hypokalaemia, congenital or acquired long QT interval.

Hypokalaemia should be corrected.

Before any administration, and if possible according to the patient's clinical status, it is recommended to monitor factors which could favour the occurrence of this rhythm disorder:
- bradycardia less than 55 bpm,
- hypokalaemia,
- congenital prolongation of the QT interval.
- on-going treatment with a medication likely to produce pronounced bradycardia (< 55 bpm), hypokalaemia, decreased intracardiac conduction, or prolongation of the QTc interval (see 4.5 Interaction with other medicinal products and other forms of interaction).

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

4.5. Interactions with other medical products and other forms of interaction

Combinations which are contraindicated

Medications which could induce torsades de pointes:
- Class Ia antiarrhythmic agents such as quinidine, disopyramide, procainamide;
- Class III antiarrhythmic agents such as amiodarone, sotalol;
- Others medications such as bepridil, cisapride, sulotropride, thioridazine, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin.

This list is not exhaustive.

Levodopa: reciprocal antagonism of effects between levodopa and neuroleptics.

**Combinations which are not recommended**

Amisulpiride may enhance the central effects of alcohol.

**Combinations which require precautions for use**

Medications which enhance the risk of torsades de pointes:
- Bradycardia-inducing medications such as beta-blockers, bradycardia-inducing calcium channel blockers such as diltiazem and verapamil, clonidine, guanfacine; digitalis;
- Medications which induce hypokalaemia: hypokalemic diuretics, stimulant laxatives, IV amphotericin B, glucocorticoids, tetracosactides;
- Neuroleptics such as pimozide, haloperidol; imipramine, antidepressants; lithium.

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 agents and other hypotensive medications;
- Dopamine agonists (eg: levodopa) since it may attenuate their action.

**4.6. Pregnancy and lactation**

In animals, amisulpride did not show direct 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.

The safety of amisulpride during human pregnancy has not been established. Therefore, use of the drug is contraindicated during pregnancy and in women of child bearing potential unless using adequate contraception.

It is not known whether amisulpride is excreted in breast milk, breast-feeding is therefore contra-indicated.

**4.7. Effects on ability to drive and use machines**

Even used as recommended, amisulpride may affect reaction time so that the ability to drive vehicles or operate machinery can be impaired.

**4.8. Undesirable effects**

The following adverse effects have been observed in controlled clinical trials. In some instances it can be difficult to differentiate adverse events from symptoms of the underlying disease.

*Common adverse effects (5-10%):*
- insomnia, anxiety, agitation

*Less common adverse effects (0.1-5%):*
- somnolence, gastrointestinal disorders such as constipation, nausea, vomiting, dry mouth.

*In common with other neuroleptics:*

Amisulpiride causes an increase in plasma prolactin levels which is reversible after drug discontinuation. This may result in galactorrhoea, amenorrhoea, gynaecomastia, breast pain, orgasmic dysfunction and impotence.

Weight gain may occur under therapy with amisulpride.

Acute dystonia (spasm torticolis, oculogyric crisis, trismus) may appear. This is reversible without discontinuation of amisulpride upon treatment with an antiparkinsonian agent.
Extrapyramidal symptoms may occur: tremor, rigidity, hypokinesia, hypersalivation, akathisia. 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.

Tardive dyskinesia characterised 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.

Hypotension and bradycardia have been reported occasionally. Cases of QT prolongation and very rare cases of torsades de pointes have been reported.

Allergic reactions, elevations of hepatic enzymes, mainly transaminases and cases of seizures have been very rarely reported.

Very rare cases of Neuroleptic Malignant Syndrome have been reported (see 4.4 Special warnings and special precautions for use).

4.9. **Overdose**
Experience with amisulpride in overdosage is limited. Exaggeration of the known pharmacological effects of the drug have been reported. These include drowsiness and sedation, coma, hypotension and extrapyramidal symptoms.

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

Since amisulpride is weakly dialysed, hemodialysis should not be used 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 the QT interval. If severe extrapyramidal symptoms occur, anticholinergic agents should be administered.

5. **PHARMACOLOGICAL PROPERTIES**

5.1. **Pharmacodynamic properties**
Pharmacotherapeutic group: Benzamides

ATC-code: N05AL

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, -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**
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 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. 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 to 3. The AUC of amisulpride in mild renal failure increased two fold and almost tenfold in moderate renal failure (see chapter 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.

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.

6. **PHARMACEUTICAL PARTICULARS**

6.1. **List of excipients**

Amisulpride 50 mg, 100 mg and 200 mg tablets contain the following excipients:

- Maize starch
- Lactose monohydrate
- Methylcellulose 400 cP
- Colloidal silica anhydrous
- Magnesium stearate

6.2. **Incompatibilities**

None known.

6.3. **Shelf life**

24 months.

6.4. **Special precautions for storage**

Store below 25°C
6.5. Nature and contents of container
PVC 250µm foil/Al 25µm foil blister packed in a cardboard carton.

6.6. Instruction for use and handling (use and disposal)
There are no special instructions for use/handling

7. MARKETING AUTHORISATION HOLDER
Technopharm Limited
Chapelizod
Dublin 20
Republic of Ireland

8. MARKETING AUTHORISATION NUMBER
PL 20176/0010

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
06/06/2006

10. DATE OF REVISION OF THE TEXT
06/06/2006
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
Amisulpride 100 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 100 mg amisulpride.

For excipients please refer to section 6.1.

3. PHARMACEUTICAL FORM
Amisulpride tablets 100 mg are white to off white, round tablets with breakline, marked with AM with the breakline in the middle (i.e. A/M) on one side and 100 on the other, diameter 9.5 mm.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
Treatment of acute and chronic schizophrenic disorders, in which positive symptoms (such as delusions, hallucinations, thought disorders) and/or negative symptoms (such as blunted affect, emotional and social withdrawal) are prominent, including patients characterised by predominant negative symptoms.

4.2. Posology and method of administration
For acute psychotic episodes, oral doses between 400 mg/d and 800 mg/d are recommended. In individual cases, the daily dose may be increased up to 1200 mg/d. Doses above 1200 mg/d have not been extensively evaluated for safety and therefore should not be used. No specific titration is required when initiating the treatment with amisulpride. 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.

For patients characterised by predominant negative symptoms, oral doses between 50 mg/d and 300 mg/d are recommended. Doses should be adjusted individually.

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

**Elderly**: Amisulpride should be used with particular caution because of a possible risk of hypotension or sedation.

**Children**: Amisulpride is contra-indicated in children under 15 years of age as its safety has not yet been established.

**Renal insufficiency**: Amisulpride is eliminated by the 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. As there is no experience in patients with severe renal impairment (CRCL < 10 ml/min) particular care is recommended in these patients. (see 4.4 Special warnings and precautions for use)

Hepatic insufficiency: since the drug is weakly metabolised a dosage reduction should not be necessary.

4.3. Contraindications
- Hypersensitivity to the active ingredient or to other ingredients of the drug;
- Concomitant prolactin-dependent tumours e.g. pituitary gland prolactinomas and breast cancer;
- Phaeochromocytoma;
- Children under 15 years of age;
- Pregnancy or lactation;
- Women of childbearing potential unless using adequate contraception.

Combination with the following medications which could induce torsades de pointes:
- Class Ia antiarrhythmic agents such as quinidine, disopyramide, procainamide;
- Class III antiarrhythmic agents such as amiodarone, sotalol;
- Others medications such as bepridil, cisapride, sulthiame, thioridazine, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin.
This list is not exhaustive.

- Combination with levodopa (see 4.5 Interactions with other medical products and other forms of interaction)

4.4. Special warnings and precautions for use

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

Amisulpride is eliminated by the renal route. In cases of severe renal insufficiency, the dose should be decreased and intermittent treatment should be prescribed (see 4.2 Posology and method of administration).

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

In elderly patients, amisulpride, like other neuroleptics, should be used with particular caution because of a possible risk of hypotension or sedation.

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. This effect, known to potentiate the risk of serious ventricular arrhythmias such as torsades de pointes is enhanced by the pre-existence of bradycardia, hypokalaemia, congenital or acquired long QT interval.

Hypokalaemia should be corrected.

Before any administration, and if possible according to the patient's clinical status, it is recommended to monitor factors which could favour the occurrence of this rhythm disorder:
- bradycardia less than 55 bpm,
- hypokalaemia,
- congenital prolongation of the QT interval.
- on-going treatment with a medication likely to produce pronounced bradycardia (< 55 bpm), hypokalaemia, decreased intracardiac conduction, or prolongation of the QTc interval (see 4.5 Interaction with other medicinal products and other forms of interaction).

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

4.5. Interactions with other medicinal products and other forms of interaction

Combinations which are contraindicated

Medications which could induce torsades de pointes:
- Class Ia antiarrhythmic agents such as quinidine, disopyramide, procainamide;
- Class III antiarrhythmic agents such as amiodarone, sotalol;
- Others medications such as bepridil, cisapride, sulthiame, thioridazine, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin.
This list is not exhaustive.

Levodopa : reciprocal antagonism of effects between levodopa and neuroleptics.

Combinations which are not recommended
Amisulpride may enhance the central effects of alcohol.

Combinations which require precautions for use
Medications which enhance the risk of torsades de pointes:
- Bradyarrhythmia-inducing medications such as beta-blockers, bradycardia-inducing calcium channel blockers such as diltiazem and verapamil, clonidine, guanfacine ; digitalis;
- Medications which induce hypokalaemia : hypokalemic diuretics, stimulant laxatives, IV amphotericin B, glucocorticoids, tetracosactides;
- Neuroleptics such as pimozide, haloperidol ; imipramine, antidepressants ; lithium.

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;
- Dopamine agonists (eg : levodopa) since it may attenuate their action.

4.6. Pregnancy and lactation
In animals, amisulpride did not show direct 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.

The safety of amisulpride during human pregnancy has not been established. Therefore, use of the drug is contraindicated during pregnancy and in women of child bearing potential unless using adequate contraception.

It is not known whether amisulpride is excreted in breast milk, breast-feeding is therefore contra-indicated.

4.7. Effects on ability to drive and use machines
Even used as recommended, amisulpride may affect reaction time so that the ability to drive vehicles or operate machinery can be impaired.

4.8. Undesirable effects
The following adverse effects have been observed in controlled clinical trials. In some instances it can be difficult to differentiate adverse events from symptoms of the underlying disease.

Common adverse effects (5-10 %):
- insomnia, anxiety, agitation

Less common adverse effects (0.1-5 %):
- somnolence, gastrointestinal disorders such as constipation, nausea, vomiting, dry mouth.

In common with other neuroleptics:
Amisulpride causes an increase in plasma prolactin levels which is reversible after drug discontinuation. This may result in galactorrhoea, amenorrhoea, gynaecomastia, breast pain, orgasmic dysfunction and impotence.

Weight gain may occur under therapy with amisulpride.

Acute dystonia (spasm torticolis, oculogyric crisis, trismus) may appear. This is reversible without discontinuation of amisulpride upon treatment with an antiparkinsonian agent.

Extrapyramidal symptoms may occur: tremor, rigidity, hypokinesia, hypersalivation, akathisia. 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.

Tardive dyskinesia characterised 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.

Hypotension and bradycardia have been reported occasionally. Cases of QT prolongation and very rare cases of torsades de pointes have been reported. Allergic reactions, elevations of hepatic enzymes, mainly transaminases and cases of seizures have been very rarely reported.

Very rare cases of Neuroleptic Malignant Syndrome have been reported (see 4.4 Special warnings and special precautions for use).

4.9. Overdose

Experience with amisulpride in overdosage is limited. Exaggeration of the known pharmacological effects of the drug have been reported. These include drowsiness and sedation, coma, hypotension and extrapyramidal symptoms. In cases of acute overdosage, the possibility of multiple drug intake should be considered.

Since amisulpride is weakly dialysed, hemodialysis should not be used 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 the QT interval. If severe extrapyramidal symptoms occur, anticholinergic agents should be administered.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Benzamides

ATC-code: N05AL

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, -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

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 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. 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 to 3. The AUC of amisulpride in mild renal failure increased two fold and almost tenfold in moderate renal failure (see chapter 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.

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.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Amisulpride 50 mg, 100 mg and 200 mg tablets contain the following excipients:
- Maize starch
- Lactose monohydrate
- Methylcellulose 400 cP
- Colloidal silica anhydrous
- Magnesium stearate

6.2. Incompatibilities
None known.

6.3. Shelf life
24 months.

6.4. Special precautions for storage
Store below 25°C
6.5. **Nature and contents of container**
PVC 250µm foil/Al 25µm foil blister packed in a cardboard carton.

6.6. **Instruction for use and handling (use, handling and disposal)**
There are no special instructions for use/handling.

7. **MARKETING AUTHORISATION HOLDER**
Technopharm Limited
Chapelizod
Dublin 20
Republic of Ireland

8. **MARKETING AUTHORISATION NUMBER**
PL 20176/0011

9. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
06/06/2006

10. **DATE OF REVISION OF THE TEXT**
06/06/2006
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
   Amisulpride 200 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
   Each tablet contains 200 mg amisulpride.
   For excipients please refer to section 6.1.

3. PHARMACEUTICAL FORM
   Amisulpride tablets 200 mg are white to off white, round tablets with break line, marked with AM with the breakline in the middle (i.e. A/M) on one side and 200 on the other, diameter 12.5 mm.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
   Treatment of acute and chronic schizophrenic disorders, in which positive symptoms (such as delusions, hallucinations, thought disorders) and/or negative symptoms (such as blunted affect, emotional and social withdrawal) are prominent, including patients characterised by predominant negative symptoms

4.2. Posology and method of administration
   For acute psychotic episodes, oral doses between 400 mg/d and 800 mg/d are recommended. In individual cases, the daily dose may be increased up to 1200 mg/d. Doses above 1200 mg/d have not been extensively evaluated for safety and therefore should not be used. No specific titration is required when initiating the treatment with amisulpride. 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.
   For patients characterised by predominant negative symptoms, oral doses between 50 mg/d and 300 mg/d are recommended. Doses should be adjusted individually.
   Amisulpride can be administered once daily at oral doses up to 300 mg, higher doses should be administered bid.
   Elderly: Amisulpride should be used with particular caution because of a possible risk of hypotension or sedation.
   Children: Amisulpride is contra-indicated in children under 15 years of age as its safety has not yet been established.
   Renal insufficiency: Amisulpride is eliminated by the 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. As there is no experience in patients with severe renal impairment (CRCL < 10 ml/min) particular care is recommended in these patients. (see 4.4 Special warnings and precautions for use)
   Hepatic insufficiency: since the drug is weakly metabolised a dosage reduction should not be necessary.

4.3. Contraindications
   - Hypersensitivity to the active ingredient or to other ingredients of the drug;
   - Concomitant prolactin-dependent tumours e.g. pituitary gland prolactinomas and breast cancer;
   - Phaeochromocytoma;
- Children under 15 years of age;
- Pregnancy or lactation;
- Women of childbearing potential unless using adequate contraception.

Combination with the following medications which could induce torsades de pointes:
- Class Ia antiarrhythmic agents such as quinidine, disopyramide, procainamide;
- Class III antiarrhythmic agents such as amiodarone, sotalol;
- Others medications such as bepridil, cisapride, sulthiamide, thioridazine, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin.
This list is not exhaustive.

- Combination with levodopa (see 4.5 Interactions with other medical products and other forms of interaction)

4.4. Special warnings and precautions for use
As with other neuroleptics, Neuroleptic Malignant Syndrome, characterized by hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated CPK, may occur. In the event of hyperthermia, particularly with high daily doses, all antipsychotic drugs including amisulpride should be discontinued.

Amisulpride is eliminated by the renal route. In cases of severe renal insufficiency, the dose should be decreased and intermittent treatment should be prescribed (see 4.2 Posology and method of administration).

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

In elderly patients, amisulpride, like other neuroleptics, should be used with particular caution because of a possible risk of hypotension or sedation.

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. This effect, known to potentiate the risk of serious ventricular arrhythmias such as torsades de pointes is enhanced by the pre-existence of bradycardia, hypokalaemia, congenital or acquired long QT interval.

Hypokalaemia should be corrected.

Before any administration, and if possible according to the patient's clinical status, it is recommended to monitor factors which could favour the occurrence of this rhythm disorder:
- bradycardia less than 55 bpm,
- hypokalaemia,
- congenital prolongation of the QT interval.
- on-going treatment with a medication likely to produce pronounced bradycardia (< 55 bpm), hypokalaemia, decreased intracardiac conduction, or prolongation of the QTc interval (see 4.5 Interaction with other medicinal products and other forms of interaction).

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

4.5. Interactions with other medicinal products and other forms of interaction
Combinations which are contraindicated
Medications which could induce torsades de pointes:
- Class Ia antiarrhythmic agents such as quinidine, disopyramide, procainamide;
- Class III antiarrhythmic agents such as amiodarone, sotalol;
- Others medications such as bepridil, cisapride, sulthiamide, thioridazine, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin.
This list is not exhaustive.

Levodopa: reciprocal antagonism of effects between levodopa and neuroleptics.

**Combinations which are not recommended**
Amisulpride may enhance the central effects of alcohol.

**Combinations which require precautions for use**

Medications which enhance the risk of torsades de pointes:
- Bradycardia-inducing medications such as beta-blockers, bradycardia-inducing calcium channel blockers such as diltiazem and verapamil, clonidine, guanfacine; digitalis;
- Medications which induce hypokalaemia: hypokalemic diuretics, stimulant laxatives, IV amphotericin B, glucocorticoids, tetracosactides;
- Neuroleptics such as pimozide, haloperidol; imipramine, antidepressants; lithium.

**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;
- Dopamine agonists (eg: levodopa) since it may attenuate their action.

**4.6. Pregnancy and lactation**

In animals, amisulpride did not show direct 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.

The safety of amisulpride during human pregnancy has not been established. Therefore, use of the drug is contraindicated during pregnancy and in women of child bearing potential unless using adequate contraception.

It is not known whether amisulpride is excreted in breast milk, breast-feeding is therefore contra-indicated.

**4.7. Effects on ability to drive and use machines**

Even used as recommended, amisulpride may affect reaction time so that the ability to drive vehicles or operate machinery can be impaired.

**4.8. Undesirable effects**

The following adverse effects have been observed in controlled clinical trials. In some instances it can be difficult to differentiate adverse events from symptoms of the underlying disease.

*Common adverse effects (5-10%):*
- insomnia, anxiety, agitation

*Less common adverse effects (0.1-5%):*
- somnolence, gastrointestinal disorders such as constipation, nausea, vomiting, dry mouth.

*In common with other neuroleptics:*
Amisulpride causes an increase in plasma prolactin levels which is reversible after drug discontinuation. This may result in galactorrhoea, amenorrhoea, gynaecomastia, breast pain, orgasmic dysfunction and impotence.

Weight gain may occur under therapy with amisulpride.

Acute dystonia (spasm torticolis, oculogyric crisis, trismus) may appear. This is reversible without discontinuation of amisulpride upon treatment with an antiparkinsonian agent.

Extrapyramidal symptoms may occur: tremor, rigidity, hypokinesia, hypersalivation, akathisia. 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.

Tardive dyskinesia characterised 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.

Hypotension and bradycardia have been reported occasionally. Cases of QT prolongation and very rare cases of torsades de pointes have been reported.

Allergic reactions, elevations of hepatic enzymes, mainly transaminases and cases of seizures have been very rarely reported.

Very rare cases of Neuroleptic Malignant Syndrome have been reported (see 4.4 Special warnings and special precautions for use).

4.9. Overdose
Experience with amisulpride in overdosage is limited. Exaggeration of the known pharmacological effects of the drug have been reported. These include drowsiness and sedation, coma, hypotension and extrapyramidal symptoms.

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

Since amisulpride is weakly dialysed, hemodialysis should not be used to eliminate the drug.

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

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Benzamides
ATC-code: N05AL

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, -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
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 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. 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 to 3. The AUC of amisulpride in mild renal failure increased two fold and almost tenfold in moderate renal failure (see chapter 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.

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.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Amisulpride 50 mg, 100 mg and 200 mg tablets contain the following excipients:
  
  * Maize starch
  * Lactose monohydrate
  * Methylcellulose 400 cP
  * Colloidal silica anhydrous
  * Magnesium stearate

6.2. Incompatibilities
None known.

6.3. Shelf life
24 months.

6.4. Special precautions for storage
Store below 25°C
6.5. **Nature and contents of container**
PVC 250µm foil/Al 25µm foil blister packed in a cardboard carton.

6.6. **Instruction for use and handling (use and disposal)**
There are no special instructions for use/handling.

7. **MARKETING AUTHORISATION HOLDER**
Technopharm Limited
Chapelizod
Dublin 20
Republic of Ireland

8. **MARKETING AUTHORISATION NUMBER**
PL 20176/0012

9. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
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10. **DATE OF REVISION OF THE TEXT**
06/06/2006
SUMMARY OF PRODUCT CHARACTERISTICS

1. **NAME OF THE MEDICINAL PRODUCT**
   Amisulpride 400 mg tablets

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**
   Each tablet contains 400 mg amisulpride.

   For excipients please refer to section 6.1.

3. **PHARMACEUTICAL FORM**
   Amisulpride tablets 400 mg are white to off white, film coated, ovoidal shaped, biconvex tablets, marked with AM with the breakline in the middle (i.e. A/M) on one side and 400 on the other.

4. **CLINICAL PARTICULARS**

   4.1. **Therapeutic indications**
   Treatment of acute and chronic schizophrenic disorders, in which positive symptoms (such as delusions, hallucinations, thought disorders) and/or negative symptoms (such as blunted affect, emotional and social withdrawal) are prominent, including patients characterised by predominant negative symptoms

   4.2. **Posology and method of administration**
   For acute psychotic episodes, oral doses between 400 mg/d and 800 mg/d are recommended. In individual cases, the daily dose may be increased up to 1200 mg/d. Doses above 1200 mg/d have not been extensively evaluated for safety and therefore should not be used. No specific titration is required when initiating the treatment with amisulpride. 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.

   For patients characterised by predominant negative symptoms, oral doses between 50 mg/d and 300 mg/d are recommended. Doses should be adjusted individually.

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

   **Elderly:** Amisulpride should be used with particular caution because of a possible risk of hypotension or sedation.

   **Children:** Amisulpride is contra-indicated in children under 15 years of age as its safety has not yet been established.

   **Renal insufficiency:** Amisulpride is eliminated by the 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. As there is no experience in patients with severe renal impairment (CRCL < 10 ml/min) particular care is recommended in these patients. (see 4.4 Special warnings and precautions for use)

   Hepatic insufficiency: since the drug is weakly metabolised a dosage reduction should not be necessary.

   4.3. **Contraindications**
   - Hypersensitivity to the active ingredient or to other ingredients of the drug;
   - Concomitant prolactin-dependent tumours e.g. pituitary gland prolactinomas and breast cancer;
   - Phaeochromocytoma;
- Children under 15 years of age;
- Pregnancy or lactation;
- Women of childbearing potential unless using adequate contraception.

Combination with the following medications which could induce torsades de pointes:
- Class Ia antiarrhythmic agents such as quinidine, disopyramide, procainamide;
- Class III antiarrhythmic agents such as amiodarone, sotalol;
- Others medications such as bepridil, cisapride, sulthiame, thioridazine, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin.
This list is not exhaustive.

- Combination with levodopa (see 4.5 Interactions with other medical products and other forms of interaction)

4.4. Special warnings and precautions for use

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

Amisulpride is eliminated by the renal route. In cases of severe renal insufficiency, the dose should be decreased and intermittent treatment should be prescribed (see 4.2 Posology and method of administration).

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

In elderly patients, amisulpride, like other neuroleptics, should be used with particular caution because of a possible risk of hypotension or sedation.

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. This effect, known to potentiate the risk of serious ventricular arrhythmias such as torsades de pointes is enhanced by the pre-existence of bradycardia, hypokalaemia, congenital or acquired long QT interval.

Hypokalaemia should be corrected.

Before any administration, and if possible according to the patient's clinical status, it is recommended to monitor factors which could favour the occurrence of this rhythm disorder:
- bradycardia less than 55 bpm,
- hypokalaemia,
- congenital prolongation of the QT interval.
- on-going treatment with a medication likely to produce pronounced bradycardia (< 55 bpm), hypokalaemia, decreased intracardiac conduction, or prolongation of the QTc interval (see 4.5 Interaction with other medicinal products and other forms of interaction).

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

4.5. Interactions with other medicinal products and other forms of interaction

Combinations which are contraindicated
Medications which could induce torsades de pointes:
- Class Ia antiarrhythmic agents such as quinidine, disopyramide, procainamide;
- Class III antiarrhythmic agents such as amiodarone, sotalol;
- Others medications such as bepridil, cisapride, sulthiame, thioridazine, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin.
This list is not exhaustive.

**Levodopa**: reciprocal antagonism of effects between levodopa and neuroleptics.

**Combinations which are not recommended**
Amisulpride may enhance the central effects of alcohol.

**Combinations which require precautions for use**
Medications which enhance the risk of torsades de pointes:
- Bradycardia-inducing medications such as beta-blockers, bradycardia-inducing calcium channel blockers such as diltiazem and verapamil, clonidine, guanfacine; digitalis;
- Medications which induce hypokalaemia: hypokalemic diuretics, stimulant laxatives, IV amphotericin B, glucocorticoids, tetracosactides;
- Neuroleptics such as pimozide, haloperidol; imipramine, antidepressants; lithium.

**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;
- Dopamine agonists (eg: levodopa) since it may attenuate their action.

4.6. **Pregnancy and lactation**
In animals, amisulpride did not show direct 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.

The safety of amisulpride during human pregnancy has not been established. Therefore, use of the drug is contraindicated during pregnancy and in women of child bearing potential unless using adequate contraception.

It is not known whether amisulpride is excreted in breast milk, breast-feeding is therefore contra-indicated.

4.7. **Effects on ability to drive and use machines**
Even used as recommended, amisulpride may affect reaction time so that the ability to drive vehicles or operate machinery can be impaired.

4.8. **Undesirable effects**
The following adverse effects have been observed in controlled clinical trials. In some instances it can be difficult to differentiate adverse events from symptoms of the underlying disease.

*Common adverse effects (5-10 %):*
- insomnia, anxiety, agitation

*Less common adverse effects (0.1-5 %):*
- somnolence, gastrointestinal disorders such as constipation, nausea, vomiting, dry mouth.

*In common with other neuroleptics:*
Amisulpride causes an increase in plasma prolactin levels which is reversible after drug discontinuation. This may result in galactorrhoea, amenorrhoea, gynaecomastia, breast pain, orgasmic dysfunction and impotence.

Weight gain may occur under therapy with amisulpride.

Acute dystonia (spasm torticolis, oculogyric crisis, trismus) may appear. This is reversible without discontinuation of amisulpride upon treatment with an antiparkinsonian agent.
Extrapyramidal symptoms may occur: tremor, rigidity, hypokinesia, hypersalivation, akathisia. 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.

Tardive dyskinesia characterised 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.

Hypotension and bradycardia have been reported occasionally. Cases of QT prolongation and very rare cases of torsades de pointes have been reported. Allergic reactions, elevations of hepatic enzymes, mainly transaminases and cases of seizures have been very rarely reported.

Very rare cases of Neuroleptic Malignant Syndrome have been reported (see 4.4 Special warnings and special precautions for use).

4.9. Overdose

Experience with amisulpride in overdosage is limited. Exaggeration of the known pharmacological effects of the drug have been reported. These include drowsiness and sedation, coma, hypotension and extrapyramidal symptoms.

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

Since amisulpride is weakly dialysed, hemodialysis should not be used 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 the QT interval. If severe extrapyramidal symptoms occur, anticholinergic agents should be administered.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Benzamides

ATC-code: N05AL

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, -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

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 $39 \pm 3$ and $54 \pm 4$ 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 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. 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 to 3. The AUC of amisulpride in mild renal failure increased two fold and almost tenfold in moderate renal failure (see chapter 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.

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.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Amisulpride 400 mg tablet contains the following excipients:
- Lactose monohydrate
- Methylcellulose 400 cP
- Sodium starch glycolate
- Magnesium stearate
- Mycrocystalline cellulose
- Methacrylate polymers (Eudragit E100)
- Titanium dioxide (E171)
- Talc
- Macrogol 6000

6.2. Incompatibilities

None known.
6.3. **Shelf life**
24 months.

6.4. **Special precautions for storage**
No special precautions for storage.

6.5. **Nature and contents of container**
PVC 250µm foil/Al 25µm foil blister packed in a cardboard carton.

6.6. **Instruction for use and handling (use, and disposal)**
There are no special instructions for use/handling.

7. **MARKETING AUTHORITY HOLDER**
Technopharm Limited
Chapelizod
Dublin 20
Republic of Ireland

8. **MARKETING AUTHORISATION NUMBER**
PL 20176/0013

9. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORITY**
06/06/2006

10. **DATE OF REVISION OF THE TEXT**
06/06/2006
UKPAR Amisulpride 50, 100, 200 and 400mg Tablets

PATIENT INFORMATION LEAFLET
Amisulpride 50mg Tablets

Please read this leaflet carefully before you start to use your tablets.
- This leaflet contains important information about your treatment. If you have any doubts or questions, or you are not sure about anything, ask your doctor or pharmacist.
- Keep this leaflet. You may need to read it again.
- Your medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

This leaflet contains the following information:
1. What are Amisulpride 50mg Tablets used for?
2. Information to read BEFORE taking Amisulpride 50mg Tablets.
3. How to take your tablets.
4. Can your tablets have any side effects?
5. Storing your tablets.

The name of your medicine is Amisulpride 50mg Tablets. These are white to off-white, round tablets with a break line and AM (AM) on one side and 50 on the other. The active substance in your tablets is amisulpride.

Other ingredients are maize starch, lactose monohydrate, methocelcelose 400E, colloidal silica anhydrous and magnesium stearate. Amisulpride 50mg Tablets come in packs of 60 tablets.

Marketing Authorisation Holder: TechnoPharm Ltd, Chapelizod, Dublin 20, Ireland.
Manufacturer: Aurobindo Pharma GmbH & Co. KG, Leingrader Strasse 7-13, 61109 Dossen, Germany or Rotterdamse Pharma GmbH, Petersfelder Str. 51-63, D-90630, Inningbronn, Germany.
Distributor: PLIVA Ltd, Vision House, Bedford Road, Peterfield, Hampshire GU32 3SB.

1. What are Amisulpride 50mg Tablets used for?
Amisulpride tablets are one of a group of medicines called neuroleptics. These are used to treat acute and chronic schizophrenia. Symptoms of this condition can include seeing, hearing or smelling things that do not exist, becoming withdrawn and having irrational beliefs or suspicions.

2. Information to read BEFORE using Amisulpride 50mg Tablets.
Please take the time to read the following information carefully as this may stop you from being able to take amisulpride tablets.

When should you NOT take Amisulpride 50mg Tablets?
Ask yourself the following questions:
- Have you ever taken a medicine containing amisulpride or any of the other ingredients listed above and had an unusual or allergic reaction?
- Do you have a history of liver or kidney disease?
- Do you have phaeochromocytoma (tumour of the adrenal gland)?
- Are you under 15 years old?
- Are you pregnant or is there a chance you may be pregnant?
- Are you breastfeeding?
- Are you likely to become pregnant?
- Are you taking a dopamine agonist e.g. levodopa used in Parkinson’s disease?
- Are you taking any medicines to treat heart problems (cardiovascular)?
- Are you taking any antibiotics e.g. erythromycin, tetracycline, penicillins or sportswear?
- Are you taking Sertindole (an antidepressant)?
- Are you taking Olanzapine which can be used to treat stomach problems e.g. heartburn?
- Are you taking Thioridazine which can be used as a tranquillizer or to treat conditions such as schizophrenia?

If the answer to any of these questions is YES and you have not already discussed this with your doctor or pharmacist, you should do so as soon as possible and before taking any tablets.

When should you take special care while taking Amisulpride 50mg Tablets?
Ask yourself the following questions:
- Do you suffer from kidney problems?
- Do you have a history of epilepsy?
- Do you suffer from Parkinson’s disease?
- Do you have a slow pulse?
- Do you have an inherited heart problem?
- Do you have low levels of potassium in your blood (hypokalaemia)?

If the answer to any of these questions is YES and you have not already discussed this with your doctor or pharmacist, you should do so as soon as possible and before taking any tablets.

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

It is important that you consult your doctor or pharmacist if you are taking any other medicine. If you are not sure whether another medicine you are taking may be one of the types listed below, check with your doctor or pharmacist. Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicine including those that you have bought without a prescription.

Tell your doctor or pharmacist if you are using any of the medicines listed below:
- Medicines that reduce the amount of white blood cells in your blood (e.g. some antibacterials, painkillers and over-the-counter allergy medicines).
- Medicines that reduce the amount of blood platelets in your blood (e.g. some antibacterials).
- Medicines that reduce the amount of potassium in your blood (e.g. some antacids).
- Medicines that reduce the amount of calcium in your blood (e.g. some antacids).

It is not recommended that you drink alcohol whilst you are taking this medicine as the effects of alcohol may be increased.

You must also inform your doctor or dentist that you are taking Amisulpride Tablets before you have an anaesthetic.

Effects on your ability to drive and use machines.
When taking this medicine you may find your reaction time is affected, so you should not drive or operate machinery until you are sure that you are not affected.

3. How to take your tablets.
It is important to take this tablets as directed by your doctor. Check the medicine label to see how many tablets to take and how often to take them. If you are not sure, ask your doctor or pharmacist.

Your dose will be chosen by your doctor to suit you. Doses can range from 50mg up to 1200mg per day. If you are taking 500mg per day or less, you should take it in one dose. If you are taking more than 300mg per day then you should split the dose in two and take half in the morning and half in the evening. If you are not sure how to take your tablets you should check with your doctor or pharmacist.

Children
Amisulpride should not be used in children under 16 years old.

Pediatric liver function
The small adult doses may be used.
Reduced kidney function
Your doctor may choose to give you a lower dose.
It is very important that you follow your doctor's instructions as to the dosage of amisulpride tablets and for how long you should continue to take your tablets. You may not start feeling better straight away but you should keep taking them for as long as your doctor tells you.

If you take too many tablets
It is important to stick to the dose on the label of your medicine. If you or someone else swallows several of these tablets all together, or you think a child has swallowed any of these tablets, contact your doctor, pharmacist or hospital emergency department immediately. Always take any tablets left over with you and also the box, as this will allow easier identification of the tablets. Symptoms of overdose may include sleepiness, coma, low blood pressure, shaking, slowed movement, increased salivation, stiffness or restlessness.

If you forget to take a dose
If you forget to take a dose, take it as soon as you remember. However, if it is nearly time for your next dose, miss the forgotten dose altogether and continue with the rest of the tablets as normal.

If you start to feel better
Even when you start to feel better it is important for you to keep on taking your tablets for as long as your doctor tells you.

4. Can your tablets have any side-effects?
Like all medicines, Amisulpride 50mg Tablets can have side-effects.

The following side effects may occur:

Frequent side effects (Occur in between 5 and 10 in every 100 patients):
Sleepiness, agitation, nervousness.

Less frequent side effects (Occur in between 1 and 50 in every 1000 patients)
Sleepiness, problems with the digestion such as constipation, feeling of being sick, dry mouth.

Other side effects which have been reported include:
- Milk production from the breasts (in women), breast pain
- Shaking of the menstrual periods
- Enlarged breasts in men
- Difficulty in reaching orgasm
- Impotence
- Weight gain
- Trembling, muscle stiffness, slowed movement or restlessness
- Excess sweats
- Low blood pressure or slow pulse
- Allergic reactions
- Confusions
- Uncontrollable movements of the face or tongue dystonic dyskinesia.

Apart from tardive dyskinesia the side effects listed above are normally reversible.

Side effects may also include neck stiffness, rolling of the eyes or lack of. Your doctor may prescribe another medicine to treat these symptoms.

If you suffer from any of the side effects listed and they are severe or prolonged or if you experience any other side effects not mentioned on this leaflet, please inform your doctor or pharmacist immediately.

Very rarely, neuroleptic medicines can cause the following effects:
- Feeling of unrenewed energy, sometimes nearly unconscious
- Unstable blood pressure (this can cause dizziness or weakness)
- Fever if your temperature is very high your doctor may stop this medicine.

If you experience these symptoms you should contact your doctor immediately and stop taking these tablets.

5. Storing your tablets
Store your tablets in the original package. Store below 25°C.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Do not use this medicine after the 'use by' date on the carton. If you have any tablets that are out of date, return them to your pharmacist for disposal.
Remember this treatment is for YOU. Only a doctor can prescribe it for you. Never give it to others.
Date of preparation: 3rd February 2006
PATIENT INFORMATION LEAFLET

Amitriptyline 100mg Tablets

Please read this leaflet carefully before you start to use your tablets.

- This leaflet contains important information about your treatment. If you have any doubts or questions, or you are not sure about anything, ask your doctor or pharmacist.
- Keep this leaflet. You may need to read it again.
- Your medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

This leaflet contains the following information:
1. Information about Amitriptyline 100mg Tablets used for?
2. Information to read BEFORE taking Amitriptyline 100mg Tablets.
3. How to take your tablets.
4. Can your tablets have any side effects?
5. Storing your tablets.

The name of your medicine is Amitriptyline 100mg Tablets. These are white to off-white, round tablets with a break line and AM (AMP) on one side and 100 on the other. The active substance in your tablets is amitriptyline.

Other ingredients are lactose monohydrate, methylcellulose 4000P, colloidal silica anhydrous and magnesium stearate. Amitriptyline 100mg Tablets come in packs of 60 tablets.

Marketing Authorisation Holder: TechnoPharma Ltd, Chapelwood, Dublin 20, Ireland.
Manufacturer: AWD, Pharma GmbH & Co. KG, Eulerstrasse 17, 01097 Dresden, Germany or Rotterdorff Pharma GmbH, Pferderheider Str 53-61, D-59920, Einridge, Germany.
Distributor: PIAm Pharma Ltd, Vision House, Bedfont Road, Bedfont, Hounslow, Middlesex TW13 7DB.

1. What are Amitriptyline 100mg Tablets used for?

Amitriptyline tablets are one of a group of medicines called tricyclic antidepressants. These are used to treat acute and chronic depressive illnesses. Symptoms of this condition can include sadness, feeling down or depressed, problems with sleep, lack of interest in personal activities, physical illness and suicidal ideas.

2. Information to read BEFORE taking Amitriptyline 100mg Tablets.

Please take the time to read the following information carefully as this may stop you from being able to take your tablets.

When should you NOT take Amitriptyline 100mg tablets?

Ask yourself the following questions:
- Have you ever taken a medicine containing amitriptyline or any of the other ingredients listed above and had an unusual or allergic reaction?
- Do you have a tumour of the pituitary gland or breast cancer?
- Do you have phaeochromocytoma (a tumour of the adrenal glands)?
- Are you under 15 years old?
- Are you pregnant or is there a chance you may be pregnant?
- Are you breastfeeding?
- Are you likely to become pregnant?
- Are you taking a dopamine agonist e.g. l-dopa used in Parkinson’s disease?
- Are you taking any medicines to treat heart problems (antihypertensives)?
- Are you taking any antibiotics e.g. erythromycin, halofantrine, pemigmatine or pipemidic acid?
- Are you taking sulphasalazine (a antiinflammatory)?
- Are you taking Cisapride which can be used to treat stomach problems e.g. heartburn?
- Are you taking Tranodazine which can be used as a tranquilizer or to treat conditions such as schizophrenia?

If the answer to any of these questions is YES and you have not already discussed this with your doctor or pharmacist, you should go to an accident and emergency department and take any tablets.

When should you take special care while taking Amitriptyline 100mg Tablets?

Ask yourself the following questions:
- Do you suffer from kidney problems?
- Do you have a history of epilepsy?
- Do you suffer from Parkinson’s disease?
- Do you have a slow pulse?
- Do you have an inherited heart problem?
- Do you have low levels of potassium in your blood (hypermagnesaemia)?

If the answer to any of these questions is YES and you have not already discussed this with your doctor or pharmacist, you should do so as soon as possible and before taking any tablets.

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

It is important that you consult your doctor or pharmacist if you are taking any other medicine. If you are not sure whether another medicine you are taking may be one of the types listed below, check with your doctor or pharmacist. Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicine including those that you have bought without a prescription.

Tell your doctor or pharmacist if you are using any of the medicines listed below:
- Medicines that act on the brain (CNS depressants) including antihistamines, antidepressants, sleeping tablets, or medicines that treat anxiety.
- Clonidine, its derivatives or other medicines to slow your heart beat, or medicines which can cause your heart beat to slow.
- Diuretics which may lower levels of potassium in your blood, or other medicines which can cause this effect.
- Receptor blockers (e.g. amitriptyline).
- Anticonvulsant or antidepressant medicines.
- Medicines which lower your blood pressure.

It is not recommended that you drink alcohol whilst you are taking this medicine as the effects of alcohol may be increased.

You must also inform your doctor or dentist that you are taking Amitriptyline Tablets before you have an anaesthetic.

Effects on your ability to drive and use machines

When taking this medication you may find your reaction time is affected, so you should not drive or operate machinery until you are sure that you are not affected.

3. How to take your tablets.

It is important to take the tablets as directed by your doctor. Check the medicine label to see how many tablets to take and how often to take them. If you are not sure about your treatment, ask your doctor or pharmacist.

Your dose will be chosen by your doctor to suit you. Dosages can range from 50mg up to 1200mg per day. If you are taking 500mg per day or less, you should take it in one dose. If you are taking more than 300mg per day then you should split the dose in two and take half in the morning and half in the evening. If you are not sure how to take your tablets you should contact your doctor or pharmacist.

Children

Amitriptyline should not be used in children under 15 years old.

Reduced first function

The usual adult dose may be used.
Reduced kidney function
Your doctor may choose to give you a lower dose.
It is very important that you follow your doctor's instructions as to the dosage of amisulpride tablets and for how long you should continue to take your tablets. You may not start feeling better straight away but you should keep taking them for as long as your doctor tells you.

If you take too many tablets
It is important to stick to the dose on the label of your medicine. If you or someone else swallows several of these tablets all together, or you think a child has swallowed any of these tablets, contact your doctor, chemist or hospital emergency department immediately. Always take any tablets left over with you and also the box, as this will allow easier identification of the tablets. Symptoms of overdose may include sleepiness, coma, low blood pressure, shaking, slowed movement, increased saliva, stiffness or restlessness.

If you forget to take a dose
If you forget to take a dose, take it as soon as you remember. However, if it is nearly time for your next dose, miss the forgotten dose altogether and continue with the rest of the tablets as normal.

If you start to feel better
Even when you start to feel better it is important for you to keep on taking your tablets for as long as your doctor tells you.

4. Can your tablets have any side-effects?
Like all medicines, Amisulpride 100mg Tablets can have side-effects.

The following side effects may occur:

Frequent side effects (Occur in between 5 and 10 in every 100 patients):
- Sleepiness, agitation, nervousness.

Less frequent side effects (Occur in between 1 and 5 in every 100 patients)
- Stomach, problems with the digestion such as constipation, feeling or being sick, dry mouth.

Other side effects which have been reported include:
- Milk production from the breasts (in women), breast pain
- Stopping of the menstrual periods
- Enlarged breasts in men
- Difficulty in reaching orgasm
- Impotence
- Weight gain
- Trembling, muscle stiffness, slowed movement or restlessness.
- Excess saliva
- Low blood pressure or dizziness
- Allergic reactions
- Convulsions
- Uncontrollable movements of the face or tongue (tardive dyskinesia).

Apart from tardive dyskinesia the side effects listed above are normally reversible.

Side effects may also include neck stiffness, rolling of the eyes or lack of. Your doctor may prescribe another medicine to treat these symptoms.

If you suffer from any of the side effects listed and they are severe or prolonged or if you experience any other side effects not mentioned in this leaflet, please inform your doctor or pharmacist immediately.

Very rarely, neuroleptic medicines can cause the following effects:
- Going into an unresponsive state, sometimes nearly unconscious
- Dilation of the pupils (this can cause dizziness or weakness)
- Fever – if your temperature is very high your doctor may stop this medicine

If you experience these symptoms you should contact your doctor immediately and stop taking these tablets.

5. Storage of your tablets
Store your tablets in the original package. Store below 25°C.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Do not use this medicine after the 'use by' date on the carton. If you have any tablets that are out of date, return them to your pharmacist for disposal.

Remember: this treatment is for YOU. Only a doctor can prescribe it for you. Never give it to others.

Date of preparation: 9th February 2006
UKPAR Amisulpride 50, 100, 200 and 400mg Tablets

PL 20176/0010-13

PATIENT INFORMATION LEAFLET
Amisulpride 200mg Tablets

Please read this leaflet carefully before you start to use your tablets.

This leaflet contains important information about your treatment. If you have any doubts or questions, or you are not sure about anything, ask your doctor or pharmacist.

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

Your medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

This leaflet contains the following information:
1. What are Amisulpride 200mg Tablets used for?
2. Information on how to use Amisulpride 200mg Tablets.
3. How to take your tablets.
4. Can your tablets have any side effects?
5. Storing your tablets.

The name of your medicine is Amisulpride 200mg Tablets. These are white to off-white, round tablets with a break line and AM (an) on one side and 200 on the other. The active substance in your tablets is amisulpride.

Other ingredients are used for tablets, with lactose monohydrate, methylcellulose 4000g, colloidal silicon dioxide and magnesium stearate. Amisulpride Tablets come in packs of 60 tablets.

Marketing Authorisation Holder: TechnoPharm Ltd, Chapeltown, Leeds, West Yorkshire, LS8 1QD, United Kingdom.
Manufacturer: AWC Pharma GmbH & Co. KG, Leipziger Straße 7-13, 01109 Dresden, Germany or Rottapharm GmbH, Peterender Str 91-93, D-59330, Emmerich, Germany.
Distributor: DLVA Pharma Ltd, Vision House, Bedford Road, Petersfield, Hampshire GU32 3QG.

1. What are Amisulpride 200mg Tablets used for?

Amisulpride tablets are one of a group of medicines called neuroleptics. These are used to treat acute and chronic schizophrenia. Symptoms of this condition can include sensing, seeing or hearing things that do not exist, becoming withdrawn and having mistaken beliefs or suspicions.

2. Information to read BEFORE taking Amisulpride 200mg Tablets.

Please take the time to read the following information carefully as this may stop you from being able to take amisulpride tablets.

When should you NOT take amisulpride 200mg tablets?

Ask yourself the following questions:

- Have you ever taken a medicine containing amisulpride or any of the other ingredients listed above and had an unusual or allergic reaction?
- Do you have a tumour of the salivary gland or breast cancer?
- Do you have phaeochromocytoma (tumour of the adrenal gland)?
- Are you under 15 years old?
- Are you pregnant or is there a chance you may be pregnant?
- Are you breastfeeding?
- Are you likely to become pregnant?
- Are you taking a dopamine agonist e.g. levodopa used in Parkinson's disease?
- Are you taking any medications to treat heart problems (arrhythmias)?
- Are you taking any antibiotics e.g. erythromycin, clarithromycin, pantomidine or saquinavir?
- Are you taking aminoglycoside antibiotics e.g. amikacin or tobramycin?
- Are you taking astatine which is used to treat stomach problems e.g. heartburn?
- Are you taking beta blockers which are used as a tranquilliser or to treat conditions such as schizophrenia?

If the answer to any of these questions is YES and you have not already discussed this with your doctor or pharmacist, you should do as soon as possible and before taking any tablets.

When should you take special care while taking Amisulpride 200mg Tablets?

Answer the following questions:

- Do you suffer from kidney problems?
- Do you have a history of epilepsy?
- Do you suffer from Parkinson's disease?
- Do you have a slow pulse?
- Do you have a heart problem?
- Do you have low levels of potassium in your blood (hyponatremia)?

If the answer to any of these questions is YES and you have not already discussed this with your doctor or pharmacist, you should do as soon as possible and before taking any tablets.

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

It is important that you consult your doctor or pharmacist if you are taking any other medicine. If you are not sure whether another medicine you are taking may be one of the types listed below, check with your doctor or pharmacist. Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicine including those that you have bought without a prescription.

Tell your doctor or pharmacist if you are using any of the medicines listed below:

- Medicines that act on the brain (CNS depressants) including anaesthetics, some antihistamines, painkillers (including narcotics), barbiturates, sleeping tablets, or medicines that treat anxiety.
- Other medicines or derivatives of medicines to slow your heart beat, or medicines which can cause your heart beat to slow.
- Diuretics which may lower levels of potassium in your blood, or other medicines which can cause this effect.
- Ampheta mine B (an antidepressant).
- Antipsychotic or antidepressant medicines.
- Medicines which lower your blood pressure.

It is not recommended that you drink alcohol whilst you are taking this medicine as the effects of alcohol may be increased.

You must also inform your doctor or dentist that you are taking Amisulpride Tablets before you have an anaesthetic.

Effects on your ability to drive and use machines.

When taking this medication you may find your reaction time is affected, so you should not drive or operate machinery until you are sure that you are not affected.

3. How to take your tablets.

It is important to take the tablets as directed by your doctor. Check the medicine label to see how many tablets to take and how often to take them. If you are not sure, ask your doctor or pharmacist.

Your dose will be chosen by your doctor to suit you. Doses can range from 50mg up to 1200mg per day. If you are taking 500mg per day or less, you should take it in one dose. If you are taking more than 300mg per day, then you should split the dose into two to take half in the morning and half in the evening.

If you are not sure how to take your tablets you should check with your doctor or pharmacist.

Children

Amisulpride should not be used in children under 15 years old.

Reduced liver function

The usual adult doses may be used.
Reduced kidney function
Your doctor may choose to give you a lower dose. It is very important that you follow your doctor’s instructions as to the dosage of amisulpride tablets and for how long you should continue to take your tablets. You may not start feeling better straight away but you should keep taking them for as long as your doctor tells you.

If you take too many tablets
It is important to stick to the dose on the label of your medicine. If you or someone else swallow a number of these tablets at once, you think a child has swallowed any of these tablets, contact your doctor, pharmacist or hospital emergency department immediately. Always take any tablets left over with you and also the box, as this will allow easier identification of the tablets. Symptoms of overdose may include sleepiness, coma, low blood pressure, shaking, slow movement, increased saliva, stiffness or restlessness.

If you forget to take a dose
If you forget to take a dose, take it as soon as you remember. However, if it is nearly time for your next dose, miss the forgotten dose altogether and continue with the rest of the tablets as normal.

If you start to feel better
Even when you start to feel better it is important for you to keep on taking your tablets for as long as your doctor tells you.

4. Can your tablets have any side-effects?
Like all medicines, Amisulpride tablets can have side-effects.

The following side effects may occur:

Frequent side effects (Occur in between 5 and 10 in every 100 patients):

- Restlessness, agitation, nervousness.

Less frequent side effects (Occur in between 1 and 50 in every 1000 patients)

- Sleepiness, problems with the digestion such as constipation, feeling or being sick, dry mouth.

Other side effects which have been reported include:

- Milk production from the breasts (in women), breast pain
- Stopping of the menstrual periods
- Enlarged breasts in men
- Difficulty in reaching orgasm
- Impotence
- Weight gain
- Trembling, muscle stiffness, slowed movement or restlessness.
- Excess saliva
- Low blood pressure or light-headedness
- Allergic reactions
- Convulsions
- Uncontrollable movements of the face or tongue (tardive dyskinesia).

Apart from tardive dyskinesia the side effects listed above are normally reversible.

Side effects may also include neck stiffness, rolling of the eyes or twitching. Your doctor may prescribe another medicine to treat these symptoms.

If you suffer from any of the side effects listed and they are severe or prolonged or if you experience any other side effects not mentioned on this leaflet, please inform your doctor or pharmacist immediately.

Very rarely, neuroleptic medicines can cause the following effects:
PATIENT INFORMATION LEAFLET
Amisulpride 400mg Tablets

Please read this leaflet carefully before you start to use your tablets.

- This leaflet contains important information about your treatment. If you have any doubts or questions, or if you are not sure about anything, ask your doctor or pharmacist.
- Keep this leaflet. You may need to read it again.
- Your medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

This leaflet contains the following information:
1. What are Amisulpride 400mg Tablets used for?
2. How to take Amisulpride 400mg Tablets.
3. Can your tablets have any side effects?
4. Storing your tablets.

The name of your medicine is Amisulpride 400mg Tablets. These are white to off-white, oval tablets with a green break line and AM (AM) on one side and 400 on the other. The active substance in your tablets is amisulpride.

Other ingredients are maize starch, lactose monohydrate, methylhydroxypropylcellulose 600P, colloidal silicon dioxide and magnesium stearate. Amisulpride 400mg Tablets come in packs of 60 tablets.

Manufactured by: PWD Chemicals GmbH & Co. KG, Leipziger Strasse 7-13, D-01097 Dresden, Germany or Rotenburg Pharma GmbH, Paulusallee 71-81, D-09370 Erfurt, Germany.

1. What are Amisulpride 400mg Tablets used for?

Amisulpride tablets are one of a group of medicines called neuroleptics. They are used to treat acute and chronic schizophrenia. Symptoms of this condition can include seeing, hearing or hearing things that do not exist, becoming withdrawn or having mistaken beliefs or suspicions.

2. Information to read BEFORE using Amisulpride 400mg Tablets.

Please take time to read the following information carefully as this may stop you from being able to take amisulpride tablets.

When should you NOT take Amisulpride 400mg tablets?

Ask yourself the following questions:
- Have you ever taken a medicine containing amisulpride or any of the other ingredients listed above and had any unusual or allergic reactions?
- Do you have a tumour of the pituitary gland or breast cancer?
- Do you have pheochromocytoma (a tumour of the adrenal gland)?
- Are you under 15 years old?
- Are you pregnant or is there a chance you may be pregnant?
- Are you breastfeeding?
- Are you likely to become pregnant?
- Are you taking any anti-depressants, e.g. fluoxetine used in Parkinson's disease?
- Are you taking any medicines to treat heart problems (arrhythmias)?
- Are you taking any antibiotics, e.g. erythromycin, tetracycline, peroridione or sarfloxacin?
- Are you taking Salbutamol (an antibiotic)?
- Are you taking Chloride which can be used to treat stomach problems, e.g. heartburn.
- Are you taking Thioridazine which can be used as a tranquilizer or to treat conditions such as schizophrenia.

If the answer to any of these questions is YES and you have not already discussed this with your doctor or pharmacist, you should do so as soon as possible and before taking any tablets.

When should you take special care while taking Amisulpride 400mg Tablets?

Ask yourself the following questions:
- Do you suffer from kidney problems?
- Do you have a history of epilepsy?
- Do you suffer from Pancreatitis disease?
- Do you have a slow pulse?
- Do you have an inherited heart problem?
- Do you have low levels of potassium in your blood (hypokalaemia)?

If the answer to any of these questions is YES and you have not already discussed this with your doctor or pharmacist, you should do so as soon as possible and before taking any tablets.

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

It is important that you consult your doctor or pharmacist if you are taking any other medicine. If you are not sure whether another medicine you are taking may be one of the types listed below, check with your doctor or pharmacist. Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicine including those that you have bought without a prescription.

Tell your doctor or pharmacist if you are using any of the medicines listed below:
- Medicines that act on the brain (e.g. antidepressants, some antibiotics, painkillers, including narcotics), barbiturates, sleeping pills, or medicines that treat anxiety.
- Cimetidine, its derivatives or other medicines to slow your heart beat, or medicines which can cause your heart beat to slow.
- Diuretics which may lower levels of potasium in your blood, or other medicines which can cause this effect.
- Amisulpride (an antipsychotic).
- Antidepressants or antidepressant medicines.
- Medicines which lower your blood pressure.

It is not recommended that you drink alcohol whilst you are taking this medicine as the effects of alcohol may be increased.

You must also inform your doctor or dentist that you are taking Amisulpride Tablets before you have an anaesthetic.

Effects on your ability to drive and use machines When taking this medicine you may find your reaction time is affected, so you should not drive or operate machinery until you are sure that you are not affected.

3. How to take your tablets.

It is important to take the tablets as directed by your doctor. Check the medicine label to see how many tablets to take and how often to take them. If you do not take your medicine properly, your treatment may not be effective.

Your dose will be chosen by your doctor to suit you. Doses can range from 50mg up to 1400mg per day. If you are taking 500mg per day or less, you should take it in one dose. If you are taking more than 300mg per day then you should split the dose in two and take half in the evening.

If you are not sure how to take your tablets you should check with your doctor or pharmacist.

Instructions for Children

Amisulpride tablets should not be used in children under 15 years old.

Reduced first function

The usual adult dose may be used.

UKPAR Amisulpride 50, 100, 200 and 400mg Tablets
PL 2017/0010-13
UKPAR Amisulpride 50, 100, 200 and 400mg Tablets

Reduced kidney function
Your doctor may choose to give you a lower dose. It is very important that you follow your doctor’s instructions as to the dosage of amisulpride tablets and for how long you should continue to take your tablets. You may not start feeling better straight away but you should keep taking them for as long as your doctor tells you.

If you take too many tablets
It is important to stick to the dose on the label of your medicine. If you or someone else误吞several of these tablets all together, or if you think a child has swallowed any of these tablets, contact your doctor, pharmacist or hospital emergency department immediately. Always take any tablets left over with you and also the box, as this will allow easier identification of the tablets. Symptoms of overdose may include sleepiness, coma, low blood pressure, shaking, slowed movement, increased saliva, stiffness or restlessness.

If you forget to take a dose
If you forget to take a dose, take it as soon as you remember. However, if it is nearly time for your next dose, miss the forgotten dose altogether and continue with the rest of the tablets as normal.

If you start to feel better
Even when you start to feel better it is important for you to keep on taking your tablets for as long as your doctor tells you.

4. Can your tablets have any side-effects?
Like all medicines, Amisulpride 400mg Tablets can have side-effects.

The following side effects may occur:

Frequent side effects: (Occur in between 5 and 10 in every 100 patients):
Sedation, agitation, nervousness.

Less frequent side effects: (Occur in between 1 and 5 in every 100 patients):
Sickness, problems with the digestion such as constipation, feeling or being sick, dry mouth.

Other side effects which have been reported include:
- Milk production from the breasts (in women), breast pain
- Stopping of the menstrual periods
- Enlarged breasts in men
- Difficulty in reaching orgasm
- Impotence
- Weight gain
- Trembling, muscle stiffness, slowed movement or restlessness.
- Excess saliva
- Low blood pressure or slow pulse
- Allergic reactions
- Constipation
- Uncontrollable movements of the face or tongue (tardive dyskinesia).

Apart from tardive dyskinesia the side effects listed above are normally reversible.

Side effects may also include nausea, dizziness, confusion, feeling of restlessness. Your doctor may prescribe another medicine to treat these symptoms.

If you suffer from any of the side effects listed and they are severe or prolonged or if you experience any other side effects not mentioned on this leaflet, please inform your doctor or pharmacist immediately.

Very rarely, neuroleptic medicines can cause the following effects:
- Going into an unresponsive state, sometimes nearly unconscious
- Unstable blood pressure (this can cause dizziness or weakness)
- Fever – if your temperature is very high your doctor may stop this medicine.

If you experience these symptoms you should contact your doctor immediately and stop taking these tablets.

5. Storing your tablets
Store your tablets in the original package. Store below 25°C. KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Do not use this medicine after the “use by” date on the carton. If you have any tablets that are out of date, return them to your pharmacist for disposal.

Remember: this treatment is for YOU. Only a doctor can prescribe it for you. Never give it to others.

Date of preparation: 16th February 2008.
Amisulpride 50mg Tablets

Each film-coated tablet contains 50mg amisulpride.

Contains lactose. Please see leaflet for further information.
For oral use as directed by the physician.
Do not store above 25°C.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN
Amisulpride 100mg Tablets

60 tablets

Each film-coated tablet contains 100mg

Contains lactose. Please see leaflet for further information.
For oral use as directed by the physician.
Do not store above 25°C.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN
Amisulpride 200mg Tablets

Each film-coated tablet contains 200mg amisulpride.

Contains lactose. Please see leaflet for further information. For oral use as directed by the physician. Do not store above 25°C. KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Amisulpride 400mg Tablets

60 tablets

Each film-coated tablet contains 400mg amisulpride.

Amisulpride 400mg Tablets

MA Holder: TechnoPharm Ltd, Chapelizod, Dublin 20, Ireland.
Distributor: PLIVA Pharma Ltd, Vision House, Bedford Rd,
Peterfield, Hampshire GU32 3QB
PL: 20176/0013

Contains lactose. Please see leaflet for further information.
For oral use as directed by the physician.
Do not store above 25°C.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN