SOLIAN® 100mg, 200mg and 400mg

Amisulpride Scored Tablets

COMPOSITION

Solian 100 mg scored tablet
Amisulpride ……..……..... 100 mg,
Solian 200 mg scored tablet
Amisulpride ……..……..... 200 mg,
Solian 400 mg scored tablet
Amisulpride ……..……..... 400 mg

PHARMACEUTICAL FORM

Solian 100 mg scored tablet:
White to off-white scored tablet engraved "AMI 100".
Solian 200 mg scored tablet:
White to off-white scored tablet engraved "AMI 200".
Solian 400 mg scored film-coated tablet:
White scored film-coated tablet engraved "AMI 400".

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS

Treatment of schizophrenia, particularly acute or chronic schizophrenic disorders, characterised by positive symptoms (e.g. delirium, hallucinations, thought disorders) and/or negative symptoms (e.g. blunted emotions, emotional and social withdrawal), including when the negative symptoms predominate.

DOSAGE AND ADMINISTRATION

Usually, if the daily dose is ≤ 400 mg, it will be administered as a once-daily intake. If the daily dose exceeds 400 mg, it will be administered as two daily intakes.

Predominantly negative episodes
The recommended dosage is 50 to 300 mg/day. Dosage should be adjusted on an individual basis. The optimum dosage is about 100 mg/day.

Mixed episodes with positive and negative symptoms
At the beginning of treatment, the dosage should be that which enables the control of positive symptoms, i.e. 400 to 800 mg/day. The dosage should then be adjusted individually as a function of the patient's response, so as to obtain the minimum effective dose.

Acute psychotic episodes
At the beginning of treatment:
- it is possible to start via the IM route for a few days, at a maximum dose of 400 mg/day, replaced thereafter with oral treatment,
- the recommended dosage via the oral route is 400 to 800 mg; the maximum dosage should never exceed 1 200 mg.

Thereafter:
- the dosage should be maintained or adjusted as a function of the patient's response.

In all cases, the dosage of maintenance therapy should be established individually
using the minimum effective dose.

Elderly subjects
Amisulpride should be used with particular caution in this patient population due to the risk of hypotension and sedation (see SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE).

Renal insufficiency
Because amisulpride is excreted via the kidneys, the dosage should be reduced by half in patients with renal insufficiency whose creatinine clearance (CrCl) is between 30 and 60 ml/min, and to one third if the creatinine clearance is between 10 and 30 ml/min.

In the absence of relevant data on patients with serious renal insufficiency (CrCl < 10 ml/min), amisulpride is contraindicated (see CONTRAINDICATIONS).

Hepatic insufficiency
Amisulpride is poorly metabolised, so it is not necessary to reduce the dose in patients with hepatic insufficiency.

CONTRAINDICATIONS

This medicinal product MUST NOT BE USED in the following situations:
- Hypersensitivity to amisulpride or any of the excipients
- Serious hypertensive events have been reported in patients with pheochromocytoma using anti-dopaminergic drugs, including some benzamides. This medicinal product should therefore not be prescribed to known or suspected pheochromocytoma carriers.
- Children under 15 years of age, because no clinical data are available
-
- Known or suspected prolactin-dependent tumour, e.g., pituitary gland prolactinomas and breast cancer (see sections Special warnings and special precautions for use and Undesirable effects)
- In combination with :
  - non-antiparkinsonian dopamine agonists (cabergoline, quinagolide),
  -
  - citalopram, escitalopram, domperidone, hydroxyzine, piperaquine (see section Interaction with other medicinal products and other forms of interactions)

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE

Special Warnings
Potential fatal neuroleptic malignant syndrome

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

Prolongation of the QT interval
Amisulpride induces a dose-dependent prolongation of the QT interval. This effect, known to potentiate the risk of onset of serious ventricular arrhythmias, particularly torsades de pointes, is worsened in patients with bradycardia, hypokalaemia, or congenital or acquired prolonged QT interval (use in combination with a drug increasing the QTc interval) (see section Undesirable effects).

- Prior to administration and depending on the patient's clinical status, it is necessary to rule out any risk factors for arrhythmias, such as:Bradycardia slower than 55 bpm,
- Hypokalaemia,
- Congenital prolongation of the QT interval,
- Ongoing treatment with a medication likely to produce pronounced bradycardia (< 55 bpm), hypokalaemia, decrease intra-cardiac conduction or prolongation of the QTc interval (see sections Contraindications and Interaction with other medicinal products and other ofrms of interactions)

An ECG should be performed as part of the initial assessment of patients requiring long-term treatment with a neuroleptic.

Stroke
In randomised clinical trials *versus* placebo performed in a population of elderly patients with dementia and treated with certain atypical antipsychotic drugs, a 3-fold increase in the risk of cerebrovascular events has been observed. The mechanism of such risk increase is not known. An increase in the risk with other antipsychotic drugs, or other populations of patients cannot be excluded. This medicinal product should be used with caution in patients with stroke risk factors.
Elderly patients with dementia
There is an increased risk of mortality in elderly patients with dementia-related psychosis treated with antipsychotic drugs.
Analyses of seventeen placebo-controlled trials (mean duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of mortality in drug-treated patients of between 1.6 to 1.7 times the risk of mortality in placebo-treated patients.

Over the course of a typical 10-week treatment period, the mortality rate in drug-treated patients was approximately 4.5%, compared to approximately 2.6% in the placebo group.

Although the causes of death in clinical trials with atypical antipsychotics were varied, most of the deaths appeared to be either cardiovascular (e.g. heart failure, sudden death) or infectious (e.g. pneumonia) in nature.

Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality.

It is unclear how much the antipsychotic drug and patient characteristics contribute to the increase in mortality found in the epidemiological studies.

Venous thromboembolism
Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotic drugs often have acquired risk factors for VTE, any potential risk factors for VTE must be identified before and during treatment with **Solian** and preventive measures should be taken if needed (see UNDESIRABLE EFFECTS).

Hyperglycemia/metabolic syndrome
Cases of hyperglycaemia or glucose intolerance and onset or exacerbation of diabetes have been reported in patients treated with certain antipsychotic drugs, including amisulpride (see UNDESIRABLE EFFECTS).
Clinical and laboratory monitoring should be performed in patients receiving treatment with Solian in compliance with current recommendations. Particular caution should be exercised in patients with diabetes mellitus or with risk factors for diabetes.

Seizures
Amisulpride can lower the seizure threshold. Therefore, patients with a history of seizures should be closely monitored during treatment with Solian.

Special populations
As amisulpride is eliminated by the renal route, the dose should be decreased in patients with renal failure or another treatment may be considered (see DOSAGE AND ADMINISTRATION). There are no data concerning patients with serious renal impairment (see DOSAGE AND ADMINISTRATION)

Amisulpride, like all antipsychotics, should be used with particular caution in elderly patients due to the potential risk of sedation and hypotension. A dose reduction may also be required in elderly patients with renal impairment (see section Dosage And administration).

As with other antidopaminergic agents, caution should be exetcised when administering amisulpride in patients with Parkinson's disease since it may cause worsening of the disease. Amisulpride should be used only if neuroleptic treatment is cannot be avoided.

Withdrawal syndrome
Withdrawal symptoms including nausea, vomiting and insomnia have been described following sudden discontinuation of high doses of antipsychotics. Recurrence of psychotic symptoms may also be observed and involuntary movement disorders (such as akathisia, dystonia and dyskinesia) have been reported with amisulpride. Therefore, gradual withdrawal of amisulpride is advisable.

Hyperprolactinemia
Amisulpride may increase prolactin levels (see section Undesirable effects). Patients with a history of hyperprolactinemia or of a potentially prolactin-dependent tumour should be closely monitored during amisulpride treatment (see section Contraindications).

Benign pituitary tumour

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

Hepatotoxicity

Severe hepatotoxicity has been reported with the use of amisulpride. Patients should be informed that any signs such as asthenia, anorexia, nausea, vomiting, abdominal pain or jaundice must be reported to a doctor immediately. Investigations including a clinical examination and liver function tests must be carried out immediately (see section 4.8).

Other
Leukopenia, neutropenia and agranulocytosis have been reported with antipsychotics, including Solian. Unexplained infections or fever may be evidence of leukopenia (see section Undesirable effects), and require immediate blood tests.
Use of this drug is not recommended in combination with alcohol, dopaminergic antiparkinsonian drugs, antiparasitics likely to induce torsades de pointes, methadone, levodopa and other neuroleptics and drugs likely to induce torsades de pointes, sodium oxybate and hydroxychloroquine (see section Interaction with other medicinal products and other forms of interactions).

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

+ Sedative drugs
Many drugs or substances can have additive depressant effects on the central nervous system and contribute to decrease in alertness. This must be taken into account for patients using amisulpride. These drugs/substances include morphine derivatives (analgesics, cough suppressants and replacement therapies), neuroleptics, barbiturates, benzodiazepines, anxiolytics other than benzodiazepines (e.g. meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserin, mirtazapine, trimipramine), sedative H1 antihistamines, centrally acting antihypertensive agents, baclofen and thalidomide.

+ Medications likely to induce torsades de pointes
This serious cardiac rhythm disorder can be caused by a number of antiarrhythmic and non-antiarrhythmic drugs. Hypokalemia (see Potassium-depleting agents) is a promoting factor, as is bradycardia (see Bradycardia-inducing drugs) or pre-existing congenital or acquired QT interval prolongation.
Medicines likely to cause this adverse effect include class Ia and III antiarrhythmics agents and certain neuroleptics.
Other agents not belonging to these classes are also involved.
For dolasetron, erythromycin, spiramycin, and vincamine, only intravenously administered forms are concerned by this interaction.
Coadministration of two torsadogenic drugs is generally contraindicated.
However, some of these torsadogenic drugs are exceptions to this as they are considered essential. In this case, coadministration is simply not recommended. These torsadogenic drugs include methadone, hydroxychloroquine, antiparasitic agents (chloroquine, halofantrine, lumefantrine, pentamidine), neuroleptics.
However, citalopram, escitalopram, domperidone, hydroxyzine and piperaquine are not among these exceptions, and are therefore contraindicated when coadministered with all torsadogenic drugs.

Contraindicated combinations
+ **Non-antiparkinsonian dopamine agonists (cabergoline, quinagolide)**
There is mutual antagonism between dopamine agonists and neuroleptics.

+ **Citalopram, escitalopram, domperidone, hydroxyzine, piperaquine**
There is an increased risk of ventricular arrhythmias, especially torsades de pointes

Inadvisable combinations

+ Antiparasitics likely to induce torsades de pointes (chloroquine, halofantrine, lumefantrine, pentamidine)
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.
If possible, one of the two treatments should be discontinued.
If coadministration cannot be avoided, a preliminary QT examination should be carried out and ECG monitoring performed.

+ Antiparkinsonian dopamine agonists (amantadine, apomorphine, bromocriptine, entacapone, lisuride, pergolide, piribedil, pramipexole, rasagiline, ropinirole, rotigotine, selegiline, tolcapone)
There is mutual antagonism between dopamine agonists and neuroleptics.
Dopamine agonists can cause or worsen psychotic disorders. If treatment with neuroleptics is required in patients with Parkinson's disease treated with dopamine agonists, these dopamine agents should be tapered off gradually (sudden discontinuation exposes the patient to a risk of "neuroleptic malignant syndrome").

+ Other medications likely to induce torsades de pointes: class Ia antiarrhythmic agents (quinidine, hydroquinidine, disopyramide) and class III antiarrhythmics (amiodarone, dronedarone, sotalol, dofetilide, ibutilide), and other drugs such as arsenic compounds, diphemanil, dolasetron IV, erythromycin IV, levofloxacin, mequitazine, mizolastine, prucalopride, vincamine IV, moxifloxacin, spiramycin IV, toremifene, vandetanib
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.

+ Other neuroleptics which could induce torsades de pointes (chlorpromazine, cyamemazine, droperidol, flupenthixol, fluphenazine, haloperidol, levomepromazine, pimozide, pipamperone, pipotiazine, sulpiride, sultopride, tiapride, zuclopenthixol)
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.

+ Alcohol (beverage or excipient)
Alcohol potentiates the sedative effects induced by this type of drug. Impaired alertness may make driving vehicles and using machines dangerous. Consumption of alcoholic beverages and medicinal products containing alcohol should be avoided.

+ Levodopa
There is mutual antagonism between levodopa and neuroleptics.
In patients with Parkinson’s disease, minimum effective doses of each of these drugs should be used.

+ Methadone
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.

+ Sodium oxybate
The central nervous depressant effect is potentiated. Impaired alertness may make driving vehicles and using machines dangerous.

+ Hydroxychloroquine
There is an increased risk of ventricular arrhythmias, especially torsades de pointes

Combinations requiring precautions for use
+ **Anagrelide**
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.
When coadministering these agents, clinical and ECG monitoring are required

+ **Azithromycin, ciprofloxacin, clarithromycin, levofloxacin, norfloxacin, roxithromycin**
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.
When coadministering these agents, clinical and ECG monitoring are required.

+ **Beta-blockers in heart failure (bisoprolol, carvedilol, metoprolol, nebivolol)**
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.
In addition, there is a vasodilator effect and risk of hypotension, particularly postural (additive effect).
Clinical and ECG monitoring are required.

+ **Bradycardia-inducing drugs (in particular class IA antiarrhythmics, beta-blockers, certain class III antiarrhythmics, certain calcium channel blockers, digitalis glycosides, pilocarpine, anticholinesterases)**
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes. Clinical and ECG monitoring are required.

+ **Potassium-depleting agents (potassium-depleting diuretics, alone or in combination, stimulant laxatives, glucocorticoids, tetracosactides and amphotericin B IV)**
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.
Any existing hypokalemia should be corrected before administration, and clinical, electrolyte and ECG monitoring implemented.

+ **Lithium**
There is a risk of neuropsychiatric signs suggestive of neuroleptic malignant syndrome or lithium poisoning. Regular clinical and laboratory monitoring are required, particularly at the start of coadministration.

+ **Ondansetron**
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.
When coadministering these agents, clinical and ECG monitoring are required.

Combinations to be taken into account
+ Antihypertensive drugs (all): Antihypertensive effect and increased risk of orthostatic hypotension (additive effect).
+ **Other sedative drugs**
The central nervous depressant effect is potentiated.
Impaired alertness may make driving vehicles and using machines dangerous.

+ **Orlistat**
There is a risk of treatment failure when the drug is coadministered with orlistat.

FERTILITY, PREGNANCY, AND LACTATION

Pregnancy

Available data on the use of amisulpride in pregnant women are limited. Therefore, the safety of amisulpride during human pregnancy has not been established.

Amisulpride crosses the placenta

Animal studies have shown reproductive toxicity (see section Preclinical safety data).

The use of amisulpride is not recommended during pregnancy and in women of child bearing potential not using effective contraception, unless the benefits of such treatment outweigh the potential risks.

Neonates exposed to antipsychotics, including Solian, during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery (see section Undesirable effects). There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress or feeding disorder. These complications have varied in severity; while in some cases symptoms have been self-limited, in other cases neonates have required intensive care unit. support and prolonged hospitalisation. Consequently, newborns should be monitored carefully.

Breastfeeding

A significant amount of amisulpride is excreted in breast milk. In some cases the amount exceeds the accepted value of 10% of the mother's weight-adjusted dose; however, blood concentrations in breast-fed infants have not been evaluated. There are inadequate data on the effects of amisulpride in neonates/infants.

The benefit of breast-feeding for the infant should be weighed against the benefit of amisulpride treatment when deciding to stop breast-feeding or to not take amisulpride.

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

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients, especially those who drive and use machines, should be warned of the risk of drowsiness or blurred vision associated with the use of this drug (see section Undesirable effects).

UNDESIRABLE EFFECTS

Undesirable effects have been grouped by frequency using the following convention: very common ≥ 1/10; common ≥ 1/100 to < 1/10; uncommon ≥ 1/1 000 to < 1/100; rare ≥ 1/10 000 to < 1/1 000; very rare < 1/10 000; not known (frequency cannot be estimated from the available data).

Blood and lymphatic system disorders
Uncommon
Leukopenia, neutropenia (see section Special warnings and special precautions for use).

Rare
Agranulocytosis (see section Special warnings and special precautions for use).

Immune system disorders
Uncommon

Allergic reactions.

Endocrine disorders
Common
Increase in plasma prolactin levels which is reversible on treatment discontinuation. This may result in the following clinical signs and symptoms: galactorrhea, amenorrhea, gynecomastia, breast pain, erectile dysfunction.

Rare
Benign pituitary tumor such as prolactinoma (see sections Contraindications and Special warnings and special precautions for use)

Metabolism and nutrition disorders
Uncommon
Hyperglycaemia, hypertriglyceridemia and hypercholesterolaemia.

Rare
Hyponatremia, syndrome of inappropriate antidiuretic hormone secretion (SIADH).

Psychiatric disorders
Common
Insomnia, anxiety, agitation, frigidity.

Uncommon
Confusion.

Nervous system disorders
Very common
Extrapyramidal symptoms may occur: tremor, hypertonia, hypersalivation, akathisia, hypokinesia, dyskinesia. These symptoms are generally moderate with optimal doses and partially reversible without discontinuation of Solian upon administration of antiparkinsonian medication.

The incidence of extrapyramidal symptoms, which are dose-related, remains very low in the treatment of patients with predominantly negative symptoms at doses of 50 to 300 mg/day.

Common
Acute dystonia (spasm torticollis, oculogyric crises, trismus, etc.) may appear. This is reversible with administration of an anticholinergic antiparkinsonian agent. Discontinuation of amisulpride treatment is not required.

Somnolence.

Uncommon
Tardive dyskinesia, characterized by involuntary movements of the tongue and/or face, has been reported, usually after long-term administration.
Anticholinergic antiparkinsonians are ineffective or may induce aggravation of the symptoms.
Seizures.

Rare

Neuroleptic malignant syndrome, which is a potentially fatal complication (see section Special warnings and special precautions for use).

Not known
Restless legs syndrome.

Eye disorders
Common
Blurred vision (see section Effects on ability to drive and use machines).

Cardiac disorders

Uncommon
Bradycardia.

Rare
QT interval prolongation, ventricular arrhythmias such as torsades de pointes, ventricular tachycardia, which may result in ventricular fibrillation or cardiac arrest, sudden death (see section Special warnings and special precautions for use).

Vascular disorders
Common
Hypotension.

Uncommon
Increase blood pressure.

Rare
Cases of venous thromboembolism, including cases of pulmonary embolism, sometimes fatal, and deep vein thrombosis, have been reported with antipsychotic drugs (see section Special warnings and special precautions for use).

Respiratory, thoracic and mediastinal disorders
Uncommon
Nasal congestion, aspiration pneumonia (mainly in association with other antipsychotic and CNS depressant).

Gastrointestinal disorders
Common
Constipation, nausea, vomiting, dry mouth.

Hepatobiliary disorder

Uncommon
hepatocellular injury

Skin and subcutaneous tissue disorders
Rare
Angioedema, urticaria.

Not known
Photosensitivity reaction

Musculoskeletal and systemic disorders
Uncommon
Osteopenia, osteoporosis.

Renal and urinary disorders
Uncommon
Urinary retention.

Injury, poisoning and procedural complications

Not known
Falls resulting from adverse effects compromising balance

Pregnancy, puerperium and perinatal conditions
Not known
Neonatal drug withdrawal syndrome (see section Fertility, pregnancy, and lactation).

Investigations
Common
Weight gain.

Uncommon
Elevation of hepatic enzymes, mainly transaminases.

OVERDOSE
To date, available data on acute amisulpride overdose are limited. The signs and symptoms reported result generally result from exaggeration of the pharmacological effects of the medicinal product, clinically presenting as: drowsiness, sedation, coma, hypotension and extrapyramidal symptoms.

Fatal outcomes have been reported, mainly in combination with other antipsychotic agents.

There is no known specific antidote to amisulpride. In the event of acute overdose, use of this drug in combination with other medicinal products should be considered and appropriate measures taken:
- Close monitoring of vital signs.
- Cardiac monitoring (risk of prolongation of QT interval) until the patient recovers.
- If severe extrapyramidal symptoms occur, anticholinergic agents should be administered.
- Since amisulpride is poorly dialysable, hemodialysis is of limited use to eliminate the drug.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties
Pharmacotherapeutic group: Antipsychotic
ATC code: N05AL05

Amisulpride is an antipsychotic drug which belongs to the class of substituted benzamides.

The pharmacodynamic profile of the drug is characterised by a selective and predominant affinity for dopamine D2 and D3 receptors in the limbic system. Amisulpride has no affinity for serotonin receptors, or other neuroreceptors such as histaminic, cholinergic and adrenergic receptors.

In animal studies, at high doses, in animal studies, amisulpride preferentially blocks the dopaminergic neurones of the mesolimbic system compared to those in the striatal system. This specific affinity could explain the predominant antipsychotic effects of amisulpride compared with its extrapyramidal effects.

At low doses, amisulpride preferentially blocks the presynaptic D2/D3 dopaminergic receptors, which could explain its action on negative symptoms.

In a controlled, double-blind study versus haloperidol in 191 patients with acute schizophrenia, improvement of secondary negative symptoms was significantly greater with amisulpride compared to haloperidol.

Pharmacokinetic properties
In humans, amisulpride shows two absorption peaks: the first is achieved rapidly, one hour post-dose, and the second three to four hours after administration.

Corresponding plasma concentrations after administration of a 50 mg dose are 39 ± 3 ng/mL (one hour post-dose) and 54 ± 4 ng/mL (between 3 and 4 hours post-dose).

The volume of distribution is 5.8 L/kg; plasma protein binding is low (16%), and no drug interactions related to plasma protein binding are suspected. Absolute bioavailability is 48%.

Amisulpride is poorly metabolised: two inactive metabolites have been identified and account for approximately 4% of the total amount of drug eliminated.

There is no accumulation of amisulpride and its pharmacokinetics remain unchanged after the administration of repeated doses.

The elimination half-life is approximately 12 hours after oral dose.

Amisulpride is eliminated unchanged in the urine. Half (50%) of an IV dose is excreted via the urine,of which 90% is eliminated in the first 24 hours.

Renal clearance is approximately 330 ml/min.

A carbohydrate-rich meal significantly decreases the AUC, T_{max} and C_{max} of amisulpride but no changes are seen after a high-fat meal. The relevance of these findings in patients receiving amisulpride treatment is not known.

Liver failure
Since amisulpride is poorly metabolised, a dose reduction is not necessary in patients with liver failure.

Kidney failure
The elimination half-life is not unchanged in patients with kidney failure while total clearance is reduced by a factor of 2.5 to 3. The AUC of amisulpride in patients with mild kidney failure is increased two-fold and almost 10-fold in patients with moderate kidney failure. Experience IS limited, and there are no available data on doses higher than 50 mg. Amisulpride is poorly dialysable.

Elderly subjects
The pharmacokinetic data available for subjects aged over 65 years show that 10 to 30% increase occurs in C_{max}, $T_{1/2}$ and AUC after a single 50-mg dose.
No data are available after repeated doses

PRECLINICAL SAFETY DATA

The toxicological profile of amisulpride is determinced by the pharmacological effects of the compound. Repeated-dose toxicity studies showed no target organ impairment. In animal studies, amisulpride had an effect on foetal growth and development at doses corresponding to an equivalent human dose of 2.000 mg/day and over in patients weighing 50 kg. There is no evidence that amisulpride has teratogenic potential. No studies have been carried out on the effect of amisulpride on the behavior of the offspring.

Carcinogenesis studies have demonstrated hormone-dependent tumours in rodents. These are not clinically relevant in human.

Decreased fertility related to the pharmacological properties of the product (prolactin-mediated effects) was observed in animals.

PHARMACEUTICAL PARTICULARS

Shelf life
3 years

Nature and contents of container
15, 30 or 150 scored tablets in blisters (PVC/aluminium).
- Not all pack sizes are available in the local market

Manufactured by:
Delpharm Dijon
6 Boulevard de l'Europe 21800 Quetigny
FRANCE

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References: CCDS v14