QUALITATIVE AND QUANTITATIVE COMPOSITION

Solian® 100 mg, scored tablets
Amisulpride ……100 mg
Solian® 400 mg, scored film-coated tablets
Amisulpride …… 400 mg

PHARMACEUTICAL FORM

Solian® 100 mg, scored tablets
White to off-white scored tablet, engraved “AMI 100”.
Solian® 400 mg, scored film-coated tablets
White scored film-coated tablet, engraved “AMI 400”.

CLINICAL PARTICULARS

Therapeutic indications

Treatment of acute or chronic schizophrenic disorders, in which positive symptoms (such as delusions, hallucinations, thought disorders) and/or negative symptoms (such as blunted emotions, emotional and social withdrawal) are pronounced, including patients with predominantly negative symptoms.

Posology and method of administration

Usually:
- if the daily dose is ≤ 400 mg, it is to be administered as a once-daily dose;
- if the daily dose exceeds 400 mg, it is to be administered as two divided doses.

Predominantly negative episodes:
Doses between 50 mg/day and 300 mg/day are recommended. Doses should be adjusted individually. The optimum dosage is about 100 mg/day.

Acute psychotic episodes
It is possible to start via the IM route for a few days, at a maximum dose of 400 mg/day, switching thereafter to oral treatment,
Oral doses between 400mg/day and 800mg/day are recommended. The maximum dose should never exceed 1200mg. Given that there has been no large-scale safety assessment of doses higher than 1200mg/day, these doses should not be used.
The dosage should be maintained or adjusted according to the patient's individual response.

In all cases, the maintenance treatment should be established individually with the minimum effective dose.

Children and adolescents

The efficacy and safety of amisulpride from the age of puberty up to 18 years has not been elucidated: available data on the use of amisulpride in adolescents with schizophrenia are limited. As a result, amisulpride is not recommended in patients from the age of puberty up to 18 years. Amisulpride is contraindicated for children under 15 years of age.

Elderly subjects

Amisulpride should be used with particular caution in this patient population due to the risk of hypotension and sedation. Dose reduction may also be required in patients with kidney failure.

Renal insufficiency
Amisulpride is eliminated via the renal route. In patients with renal insufficiency, the dose should be reduced by half when creatinine clearance (CrCl) is between 30-60 ml/min and to a third in patients with CrCl between 10-30 ml/min.
As no data on patients with serious renal insufficiency (CrCl <10 ml/min) are available, careful monitoring is recommended in this population.

Hepatic insufficiency
Since amisulpride is weakly metabolized, a dosage reduction is not necessary in patients with hepatic insufficiency.

Contraindications
This medical product MUST NOT BE USED in the following cases:

- hypersensitivity to amisulpride or to any of the excipients listed in section List of excipients,
- serious hypertensive events have been reported in patients with pheochromocytoma using antidopaminergic 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 tumors, e.g. pituitary gland prolactinomas and breast cancer (see sections Special warnings and precautions for use and Undesirable effects),
- in combination with:
    - non-antiparkinsonian dopamine agonists (cabergoline, quinagolide)
    - citalopram, escitalopram, domperidone, hydroxyzine, piperaquine (see sections Interaction with other medicinal products and other forms of interactions)

Special warnings and precautions for use

Potentially fatal neuroleptic malignant syndrome
As with other neuroleptic, neuroleptic malignant syndrome (NMS) may occur. This condition is characterized by high fever, muscle rigidity, autonomic dysfunction, impaired consciousness, rhabdomyolysis, and elevated CPK values, and is potentially fatal. If a patient develops signs and symptoms suggestive of NMS or exhibits unexplained hyperthermia, particularly at high daily doses, all antipsychotic treatments , including amisulpride, should be discontinued.
Rhabdomyolysis has also been observed in patients without neuroleptic malignant syndrome.

QT interval prolongation
Amisulpride induces a dose-dependent prolongation of the QT interval. This effect, known to potentiate the risk of serious ventricular arrhythmias, particularly of the torsades de pointes, is worsened in patients with bradycardia, hypokalemia, 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 less than 55 bpm,
- hypokalaemia,
- congenital prolongation of the QT interval,
- ongoing treatment with a medicinal likely to produced pronounced bradycardia (<55 bpm), hypokalemia, decreased intracardiac conduction or prolongation of the QTc interval (see sections Contraindications and Interaction with other medicinal products and other forms of interactions).

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

Stroke
In randomized 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 increased 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 increases in elderly patients with dementia-related psychosis treated with antipsychotic drugs.

Analysis of 17 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 the clinical trials with 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 to 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 section 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 atypical antipsychotic drugs, including amisulpride (see section 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 may 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 section Posology and method of administration). There are no data concerning patients with serious renal impairment (see section Posology and method of 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 Posology and method of administration).

As with other antidopaminergic agents, caution should be exercised 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 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 movements disorders (e.g. 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 tumor should be closely monitored during amisulpride treatment (see section Contraindications).

Benign pituitary tumor
Amisulpride may increase prolactin levels. Cases of benign pituitary tumors, 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 a pituitary tumor (such as visual field defect and headache), pituitary imaging should be performed. If a diagnosis of pituitary tumor 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 sections Undesirable effects).

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, antiparasitic likely to induce torsades de pointes, sodium oxybate and hydroxychloroquine (see section Interaction with other medicinal products and other forms of interactions).

Linked to excipients
This medicinal product contains lactose. Its use is not recommended in patients with galactose intolerance, Lapp-lactase deficiency or glucose-galactose malabsorption syndrome (rare hereditaryillnesses).
This medicinal product contains less than 1 mmol sodium (23 mg) per tablet; that is to say essentially ‘sodium-free’.

Interaction with other medicinal products and other forms of interaction

+ Sedative agents
Many drugs or substances can have additive depressant effects on the central nervous system and contribute to a decrease 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, anxiolitics other than benzodiazepines (e.g. meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserine, mirtazapine, trimipramine), sedative H1-antihistamines, centrally acting antihypertensives agents, baclofen and thalidomide.

+ Medications likely to induce torsades de pointes
This serious cardiac arrhythmia 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 including class IA and III antiarrhythmic agents and certain neuroleptics.

Other agents not belonging to these classes are also involved.
For dolasteron, 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 agonist (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 a 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 antiarrhythmicsagents (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, sertindole, sulpiride, sultopride, tiapride, zuclopenthixol).
There is an increased risk of ventricular arrhythmias, particularly torsades de pointes.

+ Alcohol (beverage of 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 of effects 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 arrhythmia, particularly torsades de pointes.
When co-administering 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 required.

+ Bradycardia-inducing drugs (in particularly 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 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 co-administration.

+ **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 consideration
+ **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 and feeding disorder. These complications have varied in severity and duration; 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.

Breast-feeding
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 precautions for use).
Rare
Agranulocytosis (see section Special warnings and 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 secrion Contraindications and Special warnings and precautions for use).

Metabolism and nutrition disorders
Uncommon
Hyperglycemia (see section Special warnings and precautions for use), hypertriglyceridemia and hypercholesterolemia.
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 with doses of 50-300 mg/day.

Common
Acute dystonia (spasmodic 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 antiparkinsonian 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 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 precautions for use).

Vascular disorders
Common
Hypotension.

Uncommon
Increase in 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 precautions for use).

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

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

Hepatobiliary disorders
Uncommon
Hepatocellular injury.

Skin and subcutaneous tissue disorders
Rare
Angioedema, urticaria
Not known
Photosensitivity reaction.

Musculoskeletal and connective tissue disorders
Uncommon
Osteopenia, osteoporosis.
Not known
Rhabdomyolysis.

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
Elevated of hepatic enzymes, mainly transaminases.

Not known
Increased blood creatine phosphokinase.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

Overdose
To date, available data on acute amisulpride overdose are limited. The signs and symptoms reported generally result from exaggeration of 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 drugs.
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 functions.
- Cardiac monitoring (risk of prolongation of the QT interval) until the patient recovers.
- If severe extrapyramidal symptoms occur, anticholinergic agents must be administered.
- Since amisulpride is poorly dialyzable, 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 characterized by a selective and predominant affinity for dopaminergic D_2 and D_3 receptors in the limbic system. Amisulpride has no affinity for serotonin receptors or other neuroreceptors such as histamine, cholinergic and adrenergic receptors.

In animal studies, at high doses, 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 D_2 / D_3 dopaminergic receptors, which could explain its effects on negative symptoms.

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

Pharmacokinetic properties
In human, amisulpride shows two absorption peaks: the first is achieved rapidly, one hour post-dose and the second between 3 and 4 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 metabolized: 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 an oral dose.

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

Renal clearance is approximately 330 ml/min.
A carbohydrate-rich meal significantly decreases the AUC, Tmax and Cmax 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 metabolized, a dose reduction is not necessary in patients with liver failure.

Kidney failure
The elimination half-life is 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 ten-fold in patients with moderate kidney failure.

Experience is limited, however, and there are no available data on doses higher than 50 mg.

Amisulpride is poorly dialyzable.

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

Preclinical safety data
The toxicological profile of amisulpride is determined 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 tumors in rodents. These are not clinical relevance in human.
Decreased fertility related to the pharmacological properties of the product (prolactin-mediated effects) was observed in animals.

PHARMACEUTICAL PARTICULARS
List of excipients
Solian 100mg: sodium starch glycolate, lactose monohydrate, microcrystalline cellulose, hypromellose and magnesium stearate

Solian 400mg: sodium starch glycolate, lactose monohydrate, microcrystalline cellulose, hypromellose, magnesium stearate, polyoxyl 40 stearate and titanium dioxide

Shelf life
3 years.

Special precautions for storage
Store below 30°C, away from heat and humidity.

Presentation
30 tablets in blister packs (PVC/aluminium).

Manufactured by
Delpharm Dijon
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France.

Revision date: June 2024 (CCDS V16 based on FR SmPC Feb23)