Sulpiride 200mg Tablets

Summary of Product Characteristics Updated 10-Sep-2018 | Wockhardt UK Ltd

1. Name of the medicinal product

Sulpiride 200mg Tablets

2. Qualitative and quantitative composition

Sulpiride 200mg.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Tablets.

Sulpiride 200mg Tablets are white circular tablets marked S200 on one face and CP on the reverse.

4. Clinical particulars

4.1 Therapeutic indications

The treatment of acute and chronic schizophrenia.

4.2 Posology and method of administration

Posology

Adults

A starting dose of 400mg to 800mg daily, given as one or two tablets twice daily (morning and early evening) is recommended.

Predominantly positive symptoms (formal thought disorder, hallucinations, delusions, incongruity of affect) respond to higher doses, and a starting dose of at least 400mg twice daily is recommended, increasing if necessary up to a suggested maximum of 1200mg twice daily. Increasing the dose beyond this level has not been shown to produce further improvement.

Predominantly negative symptoms (flattening of affect, poverty of speech, anergia, apathy, as well as depression) respond to doses below 800mg daily; therefore, a starting dose of 400mg twice daily is recommended. Reducing this dose towards 200mg twice daily will normally increase the alerting effect of sulpiride.

Patients with mixed positive and negative symptoms, with neither predominating, will normally respond to a dose of 400mg-600mg twice daily.

Elderly

The same dose ranges are applicable in the elderly, but the dose should be reduced if there is evidence of renal impairment.

Paediatric population

Clinical experience in children under 14 years of age is insufficient to permit specific recommendations.

Method of administration

For oral use.

4.3 Contraindications

Phaeochromocytoma and acute porphyria.

Hypersensitivity to sulpiride or to any of the excipients listed in section 6.1.

Concomitant prolactin-dependent tumours e.g. pituitary gland prolactinomas and breast cancer (See section 4.8 Undesirable effects).

Association with levodopa or antiparkinsonian drugs (including ropinirole) (See section 4.5 Interactions with other medicinal products and other forms of interaction).

4.4 Special warnings and precautions for use

Warnings:

Increased motor agitation has been reported at high dosage in a small number of patients: in aggressive, agitated or excited phases of the disease process, low doses of sulpiride may aggravate symptoms. Care should be exercised where mania or hypomania is present.

Extrapyramidal reactions, principally akathisia have been reported in a small number of cases. If warranted, reduction in dosage or anti-parkinsonian medication may be necessary.

As with other neuroleptics, neuroleptic malignant syndrome, a potentially fatal complication, which is characterised by hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated CPK levels, has been reported. In such an event, or in the event of hyperthermia of undiagnosed origin, all antipsychotic drugs, including sulpiride, should be discontinued.

Elderly patients are more susceptible to postural hypotension, sedation and extrapyramidal effects.

In patients with aggressive behaviour or agitation with impulsiveness, sulpiride could be given with a sedative.

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

Increased Mortality in Elderly people with dementia:

Data from two large observational studies showed that elderly people with dementia who are treated with antipsychotics are at a small increased risk of death compared with those who are not treated. There are insufficient data to give a firm estimate of the precise magnitude of the risk and the cause of the increased risk is not known.

Sulpiride is not licenced for the treatment of dementia-related behavioural disturbances.

Venous thromboembolism:

Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with Sulpiride and preventive measures undertaken.

Breast cancer:

Sulpiride may increase prolactin levels. Therefore, caution should be exercised and patients with a history or a family history of breast cancer should be closely monitored during sulpiride therapy.

Precautions:

In elderly patients, as with other neuroleptics, sulpiride should be used with particular caution (see section 4.2).

In children, efficacy and safety of sulpiride have not been thoroughly investigated. Therefore, caution should be exercised when prescribing to children (see section 4.2).

When neuroleptic treatment is absolutely necessary in a patient with Parkinson's disease, sulpiride can be used, although caution is in order.

Neuroleptics may lower the epileptogenic threshold. Cases of convulsions, sometimes in patients with no previous history, have been reported with sulpiride. Caution is advised in prescribing it for patients with unstable epilepsy, and patients with a history of epilepsy should be closely monitored during therapy with sulpiride.

In patients requiring sulpiride who are receiving anti-convulsant therapy, the dose of the anti-convulsant should not be changed.

Cases of convulsions, sometimes in patients with no previous history, have been reported.

Sulpiride has an anticholinergic effect and, therefore, should be used with caution in patients with a history of glaucoma, ileus, congenital digestive stenosis, urine retention or hyperplasia of the prostate. As with all drugs for which the kidney is the major elimination pathway, the dose should be reduced and titrated in small steps in cases of renal insufficiency.

Prolongation of the QT interval:

Sulpiride induces a prolongation of the QT interval (see section 4.8). This effect is known to potentiate the risk of serious ventricular arrhythmias such as torsade de pointes.

Before any administration, and if possible according to the patient's clinical status, it is recommended to monitor factors which could favour the occurrence of this rhythm disorder, for example:

- Bradycardia less than 55 bpm

- Electrolyte imbalance in particular 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 section 4.5)

Sulpiride should be prescribed with caution in patients presenting with these factors and patients with cardiovascular disorders which may predispose to prolongation of the QT interval.

Avoid concomitant treatment with other neuroleptics (see section 4.5).

Stroke:

In randomised clinical trials versus placebo performed in a population of elderly patients with dementia and treated with certain atypical antipsychotic drugs, a 3-fold increase of the risk of cerebrovascular events has been observed. The mechanism of such risk increase is not known. An increase in the risk with other antipsychotic drugs or other populations of patients cannot be excluded. Sulpiride should be used with caution in patients with stroke risk factors.

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

Sulpiride should be used with caution in hypertensive patients, especially in the elderly population, due to the risk of hypertensive crisis. Patients should be adequately monitored.

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

4.5 Interaction with other medicinal products and other forms of interaction

Associations contra-indicated

Levodopa, antiparkinsonian drugs (including ropinirole): reciprocal antagonism of effects between levodopa or antiparkinsonian drugs (including ropinirole) and neuroleptics.

Associations not recommended

Alcohol: Enhances the sedative effects of neuroleptics. Avoid the consumption of alcoholic beverages and drugs containing alcohol.

Combination with the following medications could induce torsades de pointes or prolong the QT interval (see section 4.4):

- Bradycardia-inducing medications such as beta-blockers, bradycardia-inducing calcium channel blockers such as diltiazem and verapamil, clonidine; digitalis

- Medications which induce electrolyte imbalance, in particular those causing hypokalaemia: hypokalaemic diuretics, stimulant laxatives, IV amphotericin B, glucocorticoids, tetracosactides.

Electrolyte imbalance should be corrected

- Class Ia antiarrhythmic agents such as quinidine, disopyramide.

- Class III antiarrhythmic agents such as amiodarone, sotalol.

- Other medications such as pimozide, haloperidol, methadone, imipramine antidepressants, lithium, cisapride, thioridazine, IV erythromycin, halofantrine, pentamidine.

Associations to be taken into account

Antihypertensive agents: antihypertensive effect and possibility of enhanced postural hypotension (additive effect).

CNS depressants including narcotics, analgesics, sedative H1 antihistamines, barbiturates, benzodiazepines and other anxiolytics, clonidine and derivatives.

Antacids or sucralfate: The absorption of sulpiride is decreased after co-administration. Therefore, sulpiride should be administered two hours before these drugs.

Lithium: Increased risk of extrapyramidal effects. Discontinuation of both drugs is recommended at first signs of neurotoxicity.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development and/or postnatal development.

In humans, very limited clinical data on exposed pregnancies are available. In almost all cases of foetal or neonatal disorders reported in the context of sulpiride use during pregnancy, alternative explanations can be suggested and seem more likely. Therefore the use of sulpiride is not recommended during pregnancy because of the limited experience.

Neonates exposed to antipsychotics (including Sulpiride 200mg Film-Coated Tablets) 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. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Breast-feeding

Sulpiride has been found in the breast milk of treated women. Therefore, breast-feeding is not recommended during treatment.

Fertility

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

4.7 Effects on ability to drive and use machines

Even used as recommended, sulpiride may cause sedation so that the ability to drive vehicles or operate machinery can be impaired (see section 4.8).

4.8 Undesirable effects

The following frequency rating is used, when applicable:

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

Blood and lymphatic system disorders (see section 4.4):

Uncommon: Leukopenia.

Not known: Neutropenia, agranulocytosis

Immune system disorders:

Not known: Anaphylactic reactions including urticaria, dyspnoea, hypotension and anaphylactic shock.

Endocrine disorders:

Common: Hyperprolactinaemia

Psychiatric disorders:

Common: Insomnia.

Not known: Confusion

Nervous system disorders:

Common: Sedation or drowsiness, extrapyramidal disorder (these symptoms are generally reversible upon administration of antiparkinsonian medication), Parkinsonism, tremor, akathisia.

Uncommon: Hypertonia, dyskinesia, and dystonia.

Rare: Oculogyric crisis.

Not known: Neuroleptic malignant syndrome, hypokinesia, tardive dyskinesia (have been reported, as with all neuroleptics, after a neuroleptic administration of more than three months. Antiparkinsonian medication is ineffective or may induce aggravation of the symptoms), convulsion.

Metabolism and nutrition disorders:

Not known: hyponatraemia, syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Cardiac disorders:

Rare: Ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia.

Not known: electrocardiogram QT prolonged, cardiac arrest, torsade de pointes, sudden death (see section 4.4).

Vascular disorders:

Uncommon: Orthostatic hypotension.

Not known: Venous embolism, pulmonary embolism, deep vein thrombosis (see section 4.4).

Respiratory, thoracic and mediastinal disorders:

Not known: pneumonia aspiration (mainly in association with other CNS depressants).

Gastrointestinal disorders:

Common: constipation

Uncommon: Salivary hypersecretion.

Hepatobiliary disorders:

Common: Hepatic enzyme increased

Skin and subcutaneous tissue disorders:

Common: Maculo-papular rash.

Musculoskeletal and connective tissue disorders:

Not known: Torticollis, trismus.

Pregnancy, puerperium and perinatal conditions:

Not known: Extrapyramidal symptoms, drug withdrawal syndrome neonatal (see section 4.6)

Reproductive system and breast disorders:

Common: Breast pain, galactorrhoea.

Uncommon: Breast enlargement, amenorrhoea, orgasm abnormal, erectile dysfunction.

Not known: Gynaecomastia.

General disorders and administration site conditions:

Common: Weight gain.

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Experience with sulpiride in overdosage is limited.

The range of single toxic doses is 1 to 16g but no deaths have occurred even at a dose of 16g.

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

Symptoms

The clinical manifestations of poisoning vary depending upon the size of the dose taken. After single doses of 1g to 3g restlessness and clouding of consciousness have been reported and (rarely) extrapyramidal symptoms. Doses of 3g to 7g may produce a degree of agitation, confusion and extrapyramidal symptoms; more than 7g can cause, in addition, coma and low blood pressure.

The duration of intoxication is generally short, the symptoms disappearing within a few hours. Comas which have occurred after large doses have lasted up to four days.

No haematological or hepatic toxicity has been reported.

Treatment

Sulpiride is partly removed by haemodialysis.

There is no specific antidote to sulpiride. Treatment is only symptomatic. Appropriate supportive measures should therefore be instituted, close supervision of vital functions and cardiac monitoring (risk of QT interval prolongation and subsequent ventricular arrhythmias) is recommended until the patient recovers.

If severe extrapyramidal symptoms occur anticholinergics should be administrated.

Overdose may be treated with alkaline osmotic diuresis and, if necessary, anti-parkinsonian drugs. Emetic drugs are unlikely to be effective. Coma needs appropriate nursing, and cardiac monitoring is recommended until the patient recovers. Emetic drugs are unlikely to be effective in sulpiride overdosage.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psycholeptics; Benzamides,

ATC code: N05AL01

Sulpiride is a member of the group of substituted benzamides, which are structurally distinct from the phenothiazines, butyrophenones and thioxanthenes.

Current evidence suggests that the actions of sulpiride hint at an important distinction between different types of dopamine receptors or receptor mechanisms in the brain.

Behaviourally and biochemically sulpiride shares with classical neuroleptics a number of properties indicative of cerebral dopamine receptor antagonism. Essential and intriguing differences include lack of catalepsy at doses active in other behavioural tests, lack of effect upon noradrenaline or 5HT turnover, negligible anticholinesterase activity, no effect on muscarinic or GABA receptor binding, and a radical difference in the binding of tritiated sulpiride to striatal preparations in-vitro, compared to ^{3}H-spiperone or ^{3}H-haloperidol. These findings indicate a major differentiation between sulpiride and classical neuroleptics, which lack such specificity.

One of the characteristics of sulpiride is its bimodal activity, as it has both antidepressant and neuroleptic properties. Schizophrenia characterised by a lack of social contact can benefit strikingly.

Mood elevation is observed after a few days treatment, followed by disappearance of the florid schizophrenic symptoms. The sedation, and lack of affect characteristically associated with classical neuroleptics of the phenothiazine or butyrophenone type are not features of sulpiride therapy.

5.2 Pharmacokinetic properties

Peak sulpiride serum levels are reached 3 - 6 hours after an oral dose. The plasma half-life in man is approximately 8 hours. Approximately 40% sulpiride is bound to plasma proteins. 95% of the compound is excreted in the urine and faeces as unchanged sulpiride.

5.3 Preclinical safety data

In long term animal studies with neuroleptic drugs including sulpiride, an increased incidence of various endocrine tumours (some of which have occasionally been malignant) has been seen in some strains of rats and mice studied. The significance of these to man is not known; there is no current evidence of any association between neuroleptic use and tumour risk in man.

6. Pharmaceutical particulars

6.1 List of excipients

Lactose

Povidone K30

Microcrystalline cellulose

Sodium starch glycollate

Magnesium stearate

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C

6.5 Nature and contents of container

Multiples of 10 or 14 tablets in strips of PVC/Aluminium foil.

Multiples of 10 or 14 tablets in polypropylene/polyethylene containers with tamper evident closures.

6.6 Special precautions for disposal and other handling

None

7. Marketing authorisation holder

Wockhardt UK Ltd

Ash Road North

Wrexham

LL13 9UF

UK

8. Marketing authorisation number(s)

PL 29831/0193

9. Date of first authorisation/renewal of the authorisation

03/03/08

10. Date of revision of the text

07/09/2018

Company Contact Details

Wockhardt UK Ltd

Address
Ash Road North, Wrexham Industrial Estate,
Wrexham, LL13 9UF

Telephone
+44 (0)1978 661 261

Fax
+44 (0)1978 660 130