Summary of Product Characteristics last updated on the eMC: 14/04/2010

SPC Chlorpromazine 50mg Tablets

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1. NAME OF THE MEDICINAL PRODUCT

Chlorpromazine 50mg Tablets.

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2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50mg of Chlorpromazine Hydrochloride B.P.

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3. PHARMACEUTICAL FORM

Round, white, film- coated tablets intended for oral administration to human beings.

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4. CLINICAL PARTICULARS

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## 4.1 Therapeutic indications

Chlorpromazine is a phenothiazine neuroleptic and is indicated in the following conditions:

1) Psychotic conditions (especially paranoid), including schizophrenia, mania and hypomania.

2) As an adjunct in the short-term management of anxiety psychomotor agitation excitement, violent or dangerously impulsive behaviour.

3) Nausea or vomiting associated with terminal illness, where other agents are ineffective or unavailable.

4) Intractable hiccup.

5) Childhood schizophrenia and autism.

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## 4.2 Posology and method of administration

Method of administration: Oral.

Dosage

Dosage varies both with the individual and with the purpose for which the drug is being used. The dosage should be low to begin with and increased, gradually, under close supervision until the optimum level of control is achieved.

Adults: Initially 25mg three times daily or 75mg at bedtime, increasing by daily amounts of 25mg to the effective maintenance dose. The usual maintenance dose is in the range of 75 to 300mg daily, although some patients may require up to 1.0g daily.

Children: Aged under 1 year: Chlorpromazine should generally not be used unless the need is life-saving.

Age 1 to 5 years: 0.5mg/kg every 4 to 6 hours to a maximum daily dosage of 40mg.

Age 6 to 12 years: 1/3 to 1/2 the adult dose to a maximum daily dosage of 75mg.

Elderly or debilitated patients: Initially 1/3 to 1/2 the usual adult dose with a more gradual increase in dosage.

Dosage in Hiccup

Adults: 25 - 50mg three to four times daily.

Children: No information available.

Dosage in nausea and vomiting of terminal illness :

Adults: 10-25mg every 4 to 6 hours.

Children: Age under 1 year: Chlorpromazine should generally not be used unless the need is life-saving.

Age 1 to 5 years: 0.5 mg/kg every 4 to 6 hours. The maximum daily dosage should not exceed 40mg.

Aged 6 to 12 years: 0.5 mg/kg every 4 to 6 hours. The maximum daily dosage should not exceed 75mg.

Elderly or debilitated patients: Initially 1/3 to ½ the adult dose. The subsequent dosage should be adjusted under close supervision to obtain control.

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## 4.3 Contraindications

Chlorpromazine is contraindicated in patients with a known hypersensitivity to the drug. Chlorpromazine is also contraindicated in comatose patients, including those under the influence of alcohol or other central nervous system depressants.

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## 4.4 Special warnings and precautions for use

Chlorpromazine should be avoided whenever possible in patients with hepatic or renal dysfunction, cardiac failure, phaeochromocytoma, hypothyroidism, bone marrow depression, epilepsy, Parkinson's disease, myasthenia gravis, prostatic hypertrophy or a history of narrow angle glaucoma.

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

Chlorpromazine should be used with caution in the elderly, especially during very hot or very cold weather because of the risk of hyper- or hypothermia.

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.

Chlorpromazine is not licensed for the treatment of dementia-related behavioural disturbances.

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## 4.5 Interaction with other medicinal products and other forms of interaction

Alcohol, barbiturates and other sedatives may intensify the CNS depressant effects of chlorpromazine and respiratory depression may occur.

The hypotensive effect of most antihypertensive agents, especially alpha-adrenoceptor blocking agents, may be exaggerated by chlorpromazine.

Chlorpromazine has mild anticholinergic activity which may be enhanced by other anticholinergic drugs.

Anticholinergic drugs may decrease the antipsychotic effect of chlorpromazine. Chlorpromazine may oppose the action of some drugs, including amphetamine, levodopa, adrenaline, clonidine and guanethidine.

Some drugs interfere with the absorption of neuroleptic agents, e.g. antacids, lithium, anti-Parkinsonian agents. Although increases or decreases have been observed in the plasma concentrations of a number of drugs, including propranolol and phenobarbitone, these were not of clinical significance.

At high dosage, chlorpromazine reduces the response to hypoglycaemic agents, which may require an increase in dosage of the latter.

Clinically significant adverse drug interactions with alcohol, guanethidine and hypoglycaemic agents are documented. Adrenaline must not be used in cases of overdosage with chlorpromazine. Other interactions are of theoretical interest and are not of a serious nature. Concomitant administration of desferrioxamine and prochlorperazine has been reported to cause a transient metabolic encephalopathy with loss of consciousness for 48 to 72 hours. The possibility of a similar occurrence with chlorpromazine exists, because it shares many of the pharmacological activities of prochlorperazine.

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## 4.6 Pregnancy and lactation

The safety of chlorpromazine in pregnancy has not been established, although the drug has been in wide use for many years without apparent ill consequence. There is evidence of harmful effects in animals. As with other drugs, chlorpromazine should be avoided during pregnancy unless it is considered essential by the physician. Labour may occasionally be prolonged by chlorpromazine and therapy should be delayed until the cervix is dilated 3 to 4cms. Possible effects on the neonate include lethargy, paradoxical hyperexcitability, tremor and low Apgar score. Chlorpromazine is excreted in breast milk and breast feeding should be suspended during

treatment.

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4.7 Effects on ability to drive and use machines

Chlorpromazine may cause drowsiness, especially during the early days of therapy, and patients should be warned not to drive or operate machinery if affected.

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4.8 Undesirable effects

Minor side effects include nasal stuffiness, dry mouth, insomnia and agitation.

Cardiovascular: Hypotension, especially postural, is relatively common and elderly patients or subjects with volume depletion are particularly susceptible. Cardiac arrhythmias have been reported in patients receiving neuroleptic agents and may be dose-related. They include atrial arrhythmia, A-V block, ventricular tachycardia and fibrillation.Pre-existing cardiac disease, hypokalaemia, concurrent use of tricyclic antidepressants and old age may predispose to development of arrhythmia. E.C.G. changes may occur, including widened QT interval, ST depression, U waves and T wave changes.

Blood: Mild leucopenia may occur in up to 30% of patients on prolonged high dosage. Agranulocytosis may occur rarely and is not dose-related. Unexplained infections or pyrexia require immediate haematological investigations.

Respiratory: Clinical doses of the neuroleptics usually have little effect on respiration. However, respiratory depression may occur in susceptible patients.

Hepatic: A very small percentage of patients may develop jaundice, which is usually transient and which may be preceded by sudden pyrexia after one to three weeks of treatment. The jaundice is obstructive in type and is frequently accompanied by an eosinophilia, indicating the allergic nature of the event. Chlorpromazine therapy should be withdrawn if jaundice occurs.

Extrapyramidal: Acute dystonic or dyskinetic reactions may occur. These are usually transitory, are commoner in children and young adults and are more likely to occur within the first four days of treatment or after dosage increases. Akathisia may occur, characteristically following large initial doses.

Neuroleptic - induced parkinsonism is commoner in adults and the elderly and usually takes weeks or months of treatment to develop. Tremor is a common sign but rigidity, akinesia or other features of parkinsonism may also occur.

If tardive dyskinesia occurs, it is usually although not always associated with prolonged or high dosage. It may occur after treatment has been discontinued. To reduce the likelihood of tardive

dyskinesia, the dosage should be kept low whenever possible.

Skin and Eyes: Various skin rashes may occur during therapy with chlorpromazine. Photosensitivity eruptions may occur and patients receiving high dosage should be advised to avoid exposure to direct sunlight. Contact skin sensitisation is a rare but serious complication in persons who frequently handle chlorpromazine preparations and particular care should be taken to avoid contact of the drug with the skin.

Ocular changes and a metallic greyish-mauve discolouration of exposed skin have been reported in some patients, mainly females, who received chlorpromazine continuously for long periods of between four and eight years.

Endocrine: Hyperprolactinaemia has been reported and may result in galactorrhoea, gynaecomastia or amenorrhoea; impotence has been reported.

Neuroleptic malignant syndrome: The syndrome may occur with use of any neuroleptic agent. Symptoms include clouding of consciousness, rigidity and other extrapyramidal effects, and autonomic dysfunction, most importantly hyperpyrexia. Treatment involves the immediate cessation of neuroleptic therapy and symptomatic management as appropriate.

Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis have been reported with antipsychotic drugs- Frequency unknown

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4.9 Overdose

Symptoms of overdosage may include drowsiness or loss of consciousness, hypotension, tachycardia, ventricular arrhythmias, acute extrapyramidal reactions and hypothermia. There is no specific antidote and treatment is essentially symptomatic and supportive. The stomach should be emptied by aspiration and lavage and activated charcoal should be given. Circulatory collapse may respond to elevation of the lower limbs, although volume expansion with intravenous fluids may be required. Use of a positive inotropic agent such as dopamine may be considered if circulatory collapse does not respond to volume expansion; peripheral vasoconstrictor agents are not generally recommended and adrenaline should be avoided.

Tachyarrhythmias usually respond to restoration of normal body temperature and correction of circulatory or metabolic disturbances. Anti-arrhythmic therapy may be considered for persistent or life-threatening arrhythmias; lignocaine should be avoided and, as far as possible, so should long-acting anti-arrhythmic drugs.

If severe dystonic reactions occur, they usually respond to procyclidine 5 to 10mg or orphenadrine 20 to 40mg given intramuscularly or intravenously. Intravenous diazepam may be used to treat convulsions.

Dantrolene sodium together with cooling and general supportive measures may be used to

treat the neuroleptic malignant syndrome.

An open airway should be maintained and artificial respiration may be required in severe cases of central nervous system depression.

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## 5. PHARMACOLOGICAL PROPERTIES

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### 5.1 Pharmacodynamic properties

Chlorpromazine is a dimethylamine derivative of phenothiazine. Although the precise mechanism where by the therapeutic effects of chlorpromazine are produced is not known, the principal pharmacological action are neuroleptic, resulting in the favourable modification of psychotic symptoms. Chlorpromazine also exerts sedative and anti-emetic activity. It has alpha-adrenergic blocking and weaker anticholinergic activities. It is an inhibitor of dopamine and it inhibits prolactine-release-inhibitory factor (considered to be dopamine), thus stimulating the release of prolactin. Chlorpromazine has serotonin blocking and weak antihistaminic properties. It inhibits the heat-regulating centre so that the subject tends to acquire the ambient temperature.

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### 5.2 Pharmacokinetic properties

Although chlorpromazine is readily absorbed from the gastrointestinal tract, it undergoes first-pass metabolism in the gut wall and is also extensively metabolised in the liver. Intramuscular administration avoids much of the first-pass metabolism of the drug. Paths of metabolism include hydroxylation and conjugation with glucuronic acid, N-oxidation, oxidation of a sulphur atom and dealkylation. Chlorpromazine is extensively bound to plasma proteins. It is widely distributed in the body and across the blood-brain barrier to achieve higher concentration in the brain than in the plasma. Chlorpromazine and its metabolism also cross the placental barrier and are excreted in breast milk. Although the plasma half-life of chlorpromazine has been reported to be only a few hours, elimination of metabolism may be very prolonged. Chlorpromazine is excreted in the urine and faeces in the form of numerous active and inactive metabolites.

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### 5.3 Preclinical safety data

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

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## 6. PHARMACEUTICAL PARTICULARS

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### 6.1 List of excipients

Lactose B.P.

Maize Starch B.P.

Povidone B.P.

Sodium Starch Glycollate B.P.

Magnesium Stearate B.P.

Opadry Y-I-7000

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### 6.2 Incompatibilities

None.

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### 6.3 Shelf life

4 years (48 months).

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### 6.4 Special precautions for storage

Store in a cool dry place.

Protect from light and heat.

Keep out of reach of children.

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6.5 Nature and contents of container

Polypropylene securitainers with tamper evident polypropylene caps.

Pack sizes: 28, 50, 100, 250, 500, 1000 and 5000 tablets.

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6.6 Special precautions for disposal and other handling

Not applicable.

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Administrative Data

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7. MARKETING AUTHORISATION HOLDER

Goldshield Pharmaceutical Ltd

NLA Tower

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Croydon

CR0 0XT

United Kingdom

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8. MARKETING AUTHORISATION NUMBER(S)

PL 12762/0109

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 July 2001

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10. DATE OF REVISION OF THE TEXT

24/02/2010

| Active Ingredients/Generics |
| --- |
| chlorpromazine hydrochloride |