

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

CHLORACTIL/Chlorpromazine HCl

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10.00 mg of Chlorpromazine HCl BP.

Excipient with known effect

Each tablet also contains 43.60 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-Coated Tablet

White, film-coated, biconvex, odourless tablets, with a break line on one side and plain on the other side.

The tablet can be divided into equal doses.

4.1 Therapeutic indications

Chlorpromazine is a phenothiazine neuroleptic. It is indicated in the following conditions:

Schizophrenia and other psychoses (especially where paranoia is a predominant symptom), mania and hypomania. In anxiety, psychomotor agitation, excitement, violent or dangerously impulsive behaviour. Chlorpromazine may be used as an adjunct in the short-term management of these conditions.

Intractable hiccup.

Nausea and vomiting in terminal illness (where other drugs have failed or are not available).

Induction of hypothermia is facilitated by Chlorpromazine Tablets which prevents shivering and causes vasodilatation.

Childhood schizophrenia and autism.

4.2 Posology and method of administration

Posology

Dosages should be low to begin with and gradually increased under close supervision until the optimum dosage for the individual is reached. Individuals vary considerably and the optimum dose may be affected by the formulation used.

Dosage of chlorpromazine in schizophrenia, other psychoses, anxiety and agitation etc.

Adult:

Initially 25 mg t.d.s. or 75 mg at bedtime increasing by daily amounts of 25 mg to an effective maintenance dose. This is usually in the range 75 to 300mg daily but some patients may require up to 1 g daily.

Children under 1 year:

Do not use unless the risk-benefit ratio has been assessed.

Children 1-5 years:

0.5 mg/kg body weight every 4-6 hours to a maximum recommended dose of 40mg daily.

Children 6-12 years:

1/3 - 1/2 adult dose to a maximum recommended dose of 75 mg daily.

Elderly or debilitated patients:

Start with 1/3 - 1/2 usual adult dose with a more gradual increase in dosage.

Hiccups

Adult:

25-50 mg t.d.s. or q.d.s.

Children under 1 year:

No information available.

Children 1-5 years:

No information available.

Children 6-12 years:
No information available.

Elderly or debilitated patients:
As for adults.

Nausea and vomiting in terminal illness:

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

Children under 1 year:
Do not use unless the risk-benefit ratio has been assessed.

Children 1-5 years:
0.5 mg/kg every 4-6 hours. Maximum daily dosage should not exceed 40 mg.

Children 6-12 years:
0.5 mg/kg every 4-6 hours. Maximum daily dosage should not exceed 75 mg.

Elderly or debilitated patients:

Initially 1/3 - 1/2 adult dose. The physician should then use his clinical judgment to obtain control.

Method of administration

For oral use.

4.3 Contraindications

- Hypersensitivity to the active substance, phenothiazines or to any of the excipients listed in section 6.1.
- Hypothyroidism.
- Cardiac failure
- .
- Pheochromocytoma.
- Myasthenia gravis.
- Risk of angle-closure glaucoma.
- Risk of urinary retention related to urethra-prostatic disorders.
- History of agranulocytosis.

- Dopaminergic antiparkinsonism agents (see section 4.5).
- Nursing mothers (see section 4.6).
- Citalopram, escitalopram.
- Gluten allergy or intolerance (see Section 4.4).

4.4 Special warnings and precautions for use

Blood Dyscrasias: All patients must be advised that, if they experience fever, sore throat or any other infection, they should inform their physician immediately and undergo a complete blood count. Treatment will be discontinued if any marked changes (hyperleucocytosis, granulocytopenia) are observed in the latter.

As agranulocytosis has been reported, regular monitoring of the complete blood count is recommended. The occurrence of unexplained infections or fever may be evidence of blood dyscrasia (see section 4.8) and requires immediate haematological investigation.

Neuroleptic malignant syndrome: treatment must be interrupted in the event of unexplained hyperpyrexia since this can be one of the signs of neuroleptic malignant syndrome (pallor, hyperthermia, disorders of autonomic function, altered consciousness, muscle rigidity). Signs of autonomic instability, such as hyperhidrosis and irregular blood pressure, can precede the onset of hyperthermia and as such constitute premonitory signs of the syndrome. While this neuroleptic-related effect can be of idiosyncratic origin, certain risk factors such as dehydration and brain damage would seem to indicate a predisposition.

Chlorpromazine should be avoided in patients with hypothyroidism, pheochromocytoma, myasthenia gravis and prostate hypertrophy. It should be avoided in patients with known hypersensitivity to phenothiazines or with a history of narrow angle glaucoma or agranulocytosis.

Acute withdrawal symptoms, including nausea, vomiting and insomnia, have very rarely been reported following the abrupt cessation of high doses of neuroleptics. Relapse may also occur, and the emergence of extrapyramidal reactions has been reported. Therefore, gradual withdrawal is advisable.

In schizophrenia, the response to neuroleptic treatment may be delayed. If treatment is withdrawn, the recurrence of symptoms may not become apparent for some time.

Neuroleptic phenothiazines may potentiate QT interval prolongation which increases the risk of onset of serious ventricular arrhythmias of the torsade de pointes type, which is potentially fatal (sudden death). QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalaemia, and congenital or acquired (i.e. drug induced) QT prolongation. If the clinical situation permits, medical and laboratory evaluations should be performed to rule out possible risk factors before initiating treatment with a neuroleptic agent and as deemed necessary during treatment (see section 4.8).

Where clinically possible, the absence of any factors favouring the onset of ventricular arrhythmias should be ensured before administration:

- bradycardia less than 55 beats per minute;
- hypokalaemia;
- hypocalcaemia
- hypomagnesaemia
- starvation
- alcohol abuse
- concomitant therapy with other drugs known to prolong the QT interval
- congenital long QT interval;
- ongoing treatment with any drug which could induce marked bradycardia (<55 beats per minute), hypokalaemia, intracardiac conduction depression or QT prolongation (see section 4.5).

With the exception of emergencies, it is recommended that the initial work up of patients receiving a neuroleptic should include an ECG.

Except under exceptional circumstances, this drug must not be administered to patients with Parkinson's disease.

The concomitant use of chlorpromazine with lithium, other QT prolonging agents, and dopaminergic antiparkinsonian agents is not recommended (see section 4.5).

The onset of paralytic ileus, potentially indicated by abdominal bloating and pain, must be treated as an emergency (see section 4.8).

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

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. Chlorpromazine should be used with caution in patients with stroke risk factors.

Elderly Patients with Dementia: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5% compared to a rate of about 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. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patient is not clear.

As with all anti-psychotic drugs, Chlorpromazine should not be used alone where depression is predominant. However, it may be combined with antidepressant therapy to treat those conditions in which depression and psychosis coexist.

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

Because of the risk of photosensitisation, patients should be advised to avoid exposure to direct sunlight (see section 4.8). In those frequently handling preparations of phenothiazines, the greatest care must be taken to avoid contact of the drug with the skin.

Hyperglycaemia or intolerance to glucose has been reported in patients treated with Chlorpromazine. Patients with an established diagnosis of diabetes mellitus or with risk factors for the development of diabetes who are started on Chlorpromazine should get appropriate glycaemic monitoring during treatment (see section 4.8).

The following populations must be closely monitored after administration of chlorpromazine:

- epileptics, since chlorpromazine may lower the seizure threshold. Treatment must be discontinued if seizures occur.
- elderly patients presenting with heightened susceptibility to orthostatic hypotension, sedation and extrapyramidal effects; chronic constipation (risk of paralytic ileus), and potentially prostatic hypertrophy. It should be used with caution particularly during very hot or cold weather (risk of hyper-, hypothermia).
- patients presenting with certain forms of cardiovascular disease, since this class of drug has

quinidine-like effects and can induce tachycardia and hypotension.

- patients with severe liver and/or renal failure because of the risk of accumulation.

Patients on long-term treatment should receive regular ophthalmological and haematological examinations.

Patients are strongly advised not to consume alcohol and alcohol-containing drugs throughout treatment (see section 4.5).

Treatment should be discontinued immediately and another anti-psychotic drug should be considered as an alternative in the following situation:

- Severe liver toxicity
 - Severe liver toxicity, resulting sometimes in death, has been reported with chlorpromazine use. Patients or caregivers should immediately report signs and symptoms such as asthenia, anorexia, nausea, vomiting, abdominal pain or icterus to a physician. Investigations including clinical examination and biological assessment of liver function should be undertaken immediately (see section 4.8).
- Eosinophilia
 - The presence of eosinophilia may indicate an allergic reaction to chlorpromazine. A thorough clinical examination and a repeat complete blood count (CBC) with differential count to confirm the presence of eosinophilia should be performed (see section 4.8).
- Drug reaction with eosinophilia and systemic symptoms
 - Drug reaction with eosinophilia and systemic symptoms (DRESS) which can be lifethreatening or fatal, have been reported in association with chlorpromazine treatment.
 - At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, chlorpromazine should be withdrawn immediately and not be restarted.

Excipient(s) with known effect

- *Lactose*: Chlorpromazine tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- *Sodium*: This medicine contains less than 1 mmol sodium (23mg) per 10 mg tablet, that is to say essentially 'sodium-free'.

Paediatric population

Since there is a potential to impact on cognitive function, children should undergo a yearly clinical examination to evaluate learning capacity. The dosage should be adjusted regularly as a function of the clinical status of the child.

4.5 Interaction with other medicinal products and other forms of interaction

Combinations contraindicated

Dopaminergics (quinagolide, cabergoline), not including dopaminergic antiparkinsonism agents, are contraindicated (see Section 4.3): reciprocal antagonism of the dopaminergic agent and neuroleptic.

Combinations not recommended

Dopaminergic antiparkinsonism agents (amantadine, bromocriptine, cabergoline, levodopa, lisuride, pergolide, pramipexole, ropinirole) are not recommended: reciprocal antagonism of the antiparkinsonism agent and neuroleptic (see Section 4.4). Neuroleptic-induced extrapyramidal syndrome should be treated with an anticholinergic rather than a dopaminergic antiparkinsonism agent (dopaminergic receptors blocked by neuroleptics).

Levodopa: reciprocal antagonism of levodopa and the neuroleptic. In Parkinson's patients, it is recommended to use the minimal doses of each drug.

QT prolonging drugs: there is an increased risk of arrhythmias when chlorpromazine is used with concomitant QT prolonging drugs (including certain anti-arrhythmics, and other antipsychotics including sultopride) and drugs causing electrolyte imbalance (see section 4.4).

Alcohol: alcohol potentiates the sedative effect of neuroleptics. Changes in alertness can make it dangerous to drive or operate machinery. Alcoholic beverages and medication containing alcohol should be avoided (see section 4.4).

Lithium (high doses of neuroleptics): concomitant use can cause confusional syndrome, hypertonia and hyper-reflexivity, occasionally with a rapid increase in serum concentrations of lithium (see section 4.4).

Combinations requiring precautions

Anti-diabetic agents: concomitant administration of high chlorpromazine doses (100 mg/day), and anti-diabetic agents can lead to an increase in blood sugar levels (decreased insulin release). Forewarn the patient and advise increased selfmonitoring of blood and urine levels. If necessary, adjust the anti-diabetic dosage during and after discontinuing neuroleptic treatment.

Topical gastrointestinal agents (magnesium, aluminium and calcium salts, oxides and hydroxides): decreased GI absorption of phenothiazine neuroleptics. Do not administer phenothiazine neuroleptics simultaneously with topical GI agents (administer more than 2 hours apart if possible).

Combinations to be taken into consideration

Antihypertensive agents: potentiation of the antihypertensive effect and risk of orthostatic hypotension (additive effects). Phenothiazines enhance the hypotensive effect of anaesthetics and calcium channel blockers. Severe postural hypotension may occur with concomitant administration of chlorpromazine and ACE inhibitors.

Atropine and other atropine derivatives: imipramine antidepressants, histamine H1-receptor antagonists, anticholinergic, antiparkinsonism agents, atropinic antispasmodics, disopyramide: build-up of atropine-associated adverse effects such as urinary retention, constipation, dry mouth.

Other CNS depressants: morphine derivatives (analgesics, antitussives and substitution treatments), barbiturates, benzodiazepines, anxiolytics other than benzodiazepines, antihypertensive agents increased central depression. Respiratory depression may occur. Changes in alertness can make it dangerous to drive or operate machinery.

The action of some drugs may be opposed by Chlorpromazine; these include amphetamine, levodopa, clonidine, guanethidine and adrenaline.

Anticholinergic drugs may reduce the antipsychotic effect of Chlorpromazine and the mild anticholinergic effect of Chlorpromazine may be enhanced by other anticholinergic drugs possibly leading to constipation, heat stroke etc. Some drugs interfere with absorption of neuroleptic agents; antacids, anti-Parkinson.

Documented clinically significant adverse interactions occur with alcohol, guanethidine and hypoglycaemic agents.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is inadequate evidence of the safety of chlorpromazine in human pregnancy.

A large amount of exposure to chlorpromazine during pregnancy did not reveal any teratogenic effect. However, there is evidence of harmful effects in animals, so like other drugs, it should be avoided in pregnancy unless the physician considers it essential. It may occasionally prolong labour and at such a time should be withheld until the cervix is dilated 3-4cm.

It is advised to keep an adequate maternal psychic balance during pregnancy in order to avoid decompensation. If a treatment is necessary to ensure this balance, the treatment should be started or continued at effective dose all through the pregnancy.

Neonates exposed to antipsychotics (including chlorpromazine) 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, bradycardia, tachycardia, feeding disorder. Consequently, newborns should be monitored carefully.

Breast-feeding

Chlorpromazine being excreted in milk, breast-feeding is not recommended during treatment.

Fertility

A decrease in fertility was observed in female animals treated with chlorpromazine. In male animals, data are insufficient to assess fertility.

In humans, because of the interaction with dopamine receptors, chlorpromazine may cause hyperprolactinaemia which can be associated with impaired fertility in women (see section 4.8). In men, data on consequences of hyperprolactinaemia are insufficient with regard to fertility.

4.7 Effects on ability to drive and use machines

The attention of patients, particularly drivers and machine operators, should be drawn to the risk of drowsiness with this medication especially at the start of treatment.

4.8 Undesirable effects

The following undesired events, listed by body system, have been reported with the following frequencies: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

System Organ Class	Very common ($\geq 1/10$)	Common ($\geq 1/100$ to $< 1/10$)	Not known (cannot be estimated from available data)
Blood and lymphatic system disorders			Agranulocytosis Leukopenia Eosinophilia Thrombocytopenia
Immune system disorders			Systemic lupus erythematosus Antinuclear antibody positive ¹ Bronchospasm Anaphylactic reacti

System Organ Class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Not known (cannot be estimated from available data)
Endocrine disorders		Hyperprolactinaemia Amenorrhoea	Galactorrhoea Gynaecomastia Erectile dysfunction Impotence Female sexual arousal disorder
Metabolism and nutrition disorders	Weight increased	Glucose tolerance impaired (see section 4.4)	Hyperglycaemia (see section 4.4) Hypertriglyceridaemia Hyponatraemia Inappropriate antidiuretic hormone secretion
Psychiatric disorders		Anxiety	Lethargy Mood altered
Nervous system disorders	Sedation ² Somnolence ² Dyskinesia (acute dystonias or dyskinesias, usually transitory are more common in children and young adults and usually occur within the first 4 days of treatment or after dosage increases) Tardive dyskinesia ³ Extrapyramidal disorder Akathisia often after large initial dose	Hypertonia Convulsion	Torticollis Oculogyric crisis Trismus Akinesia Hyperkinesia Neuroleptic malignant syndrome (hyperthermia, rigidity, autonomic dysfunction, altered consciousness) (see section 4.4.) Parkinsonism (more common in adults and elderly. It usually develops after weeks to months of treatment) include tremor, rigidity, other features of Parkinsonism
Eye disorders			Accommodation disorder ⁴ Deposit eye ⁵ Ocular changes ⁷
Cardiac disorders		ECG changes include Electrocardiogram QT	Cardiac arrhythmias, including ventricular

System Organ Class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Not known (cannot be estimated from available data)
		prolonged (as with other neuroleptics) (see section 4.4), ST depression, U-Wave and T-Wave changes.	arrhythmia, A-V block, Ventricular fibrillation, Ventricular tachycardia, Torsade de pointes, Cardiac arrest have been reported during neuroleptic phenothiazine therapy possibly related to drug. Pre-existing cardiac disease, old age, hypokalaemia and concurrent tricyclic antidepressants may predispose. Sudden death/sudden cardiac death (with possible causes of cardiac origin as well as cases of unexplained sudden death in patients receiving neuroleptic phenothiazines) (see section 4.4)
Vascular disorders	Orthostatic hypotension (Elderly or volume depleted subjects are particularly susceptible: it is more likely to occur after intramuscular administration)		Embolism venous Pulmonary embolism (sometimes fatal) Deep vein thrombosis (see section 4.4)
Respiratory, thoracic and mediastinal disorders			Respiratory depression Nasal stuffiness
Gastrointestinal disorders	Dry mouth Constipation (see section 4.4)		Colitis ischaemic Ileus paralytic (see section 4.4) Intestinal perforation (sometimes fatal) Gastrointestinal necrosis (sometimes fatal) Necrotising colitis (sometimes fatal)

System Organ Class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Not known (cannot be estimated from available data)
			Intestinal obstruction
Hepatobiliary disorders			Jaundice cholestatic Hepatocellular liver injury ⁶ Cholestatic liver injury Mixed liver injury
Skin and subcutaneous tissue disorders			Dermatitis allergic Angioedema Contact skin sensitization may occur rarely in frequently handling preparations of chlorpromazine (see section 4.4) Skin rashes Urticaria Photosensitivity reactions
Renal and urinary disorders			Urinary retention ⁴
Pregnancy, puerperium and perinatal conditions			Drug withdrawal syndrome neonatal (see section 4.6)
Reproductive system and breast disorders			Priapism
General disorders and administration site conditions			Temperature regulation disorder Insomnia Agitation

¹ may be seen without evidence of clinical disease.

² particularly at the start of treatment.

³ particularly during long term treatment; may occur after the neuroleptic is withdrawn and resolve after reintroduction of treatment or if the dose is increased.

⁴ linked to anticholinergic effects.

⁵ in the anterior segment of the eye caused by accumulation of the drug but generally without any impact on sight.

⁶ A premonitory sign may be a sudden onset of fever after one to three weeks of treatment followed by the development of jaundice. Chlorpromazine jaundice has the biochemical and other characteristics of obstructive (cholestatic) jaundice and is associated with obstructions

of the canaliculi by bile thrombi; the frequent presence of an accompanying eosinophilia indicates the allergic nature of this phenomenon. Cases of hepatocellular, cholestatic and mixed Liver injury, sometimes fatal, has been reported rarely in patients treated with chlorpromazine. Treatment should be withheld on the development of jaundice (see section 4.4).

7 the development of a metallic greyish-mauve coloration of exposed skin has been noted in some individuals, mainly females, who have received chlorpromazine continuously for long periods (4 – 8 years).

Reporting of suspected adverse reactions

Reporting 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

Toxicity and treatment of overdosage

Symptoms of chlorpromazine overdosage include drowsiness or loss of consciousness, hypotension, tachycardia, E.C.G. changes, ventricular arrhythmias, hypothermia, Parkinsonism, convulsions and coma. Severe extra-pyramidal dyskinesias may occur.

Treatment should be symptomatic with continuous respiratory and cardiac monitoring (risk of prolonged QT interval) until the patient's condition resolves.

If the patient is seen sufficiently soon (up to 6 hours) after ingestion of a toxic dose, gastric lavage may be attempted. Pharmacological induction of emesis is unlikely to be of any use. Activated charcoal should be given. There is no specific antidote. Treatment is supportive.

Generalised vasodilation may result in circulatory collapse; raising the patient's legs may be sufficient in mild hypotension but, in severe cases, volume expansion by intravenous fluids may be needed; infusion fluids should be warmed before administration in order not to aggravate hypothermia.

Positive inotropic agents such as dopamine may be tried if fluid replacement is insufficient to correct the circulatory collapse. Avoid the use of adrenaline.

Ventricular or supraventricular tachy-arrhythmias usually respond to restoration of normal body temperature and correction of circulatory or metabolic disturbances. If persistent or life threatening, appropriate anti-arrhythmic

therapy may be considered. Avoid lidocaine and, as far as possible, long acting anti-arrhythmic drugs.

Pronounced central nervous system depression requires airway maintenance or, in extreme circumstances, assisted respiration. Severe dystonic reactions usually respond to procyclidine (5-10 mg) or orphenadrine (20-40 mg) administered intramuscularly or intravenously. Convulsions should be treated with intravenous diazepam.

Neuroleptic malignant syndrome should be treated with cooling. Dantrolene sodium may be tried.

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Antipsychotics, ATC Code: N05AA01.

Chlorpromazine is a phenothiazine neuroleptic.

Chlorpromazine has depressant actions on the Central Nervous System, with alpha-adrenergic blocking and anticholinergic activities. It inhibits dopamine and prolactin release-inhibitory factor, thus stimulating the release of prolactin. It increases the turnover of dopamine in the brain.

It has anti-emetic, anti-pruritic, serotonin-blocking and weak anti-histamine properties and slight ganglion blocking activity. It inhibits the heat regulating centre in the brain and is analgesic and can relax skeletal muscle.

Due to its action on the autonomic system, it produces vasodilation, hypotension and tachycardia.

Salivary and gastric secretions are reduced.

5.2 Pharmacokinetic properties

Chlorpromazine is rapidly absorbed in the gastro-intestinal tract. It is subject to first pass metabolism in the gut wall. It is extensively metabolised in the liver and excreted in the urine and faeces. The plasma half-life is only a few hours but it has a prolonged terminal elimination phase of up to about 3 weeks.. Chlorpromazine is extensively bound to plasma protein.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:

Lactose Monohydrate
Maize Starch
Povidone K 30
Sodium Starch Glycollate
Colloidal Anhydrous Silica
Magnesium Stearate

Coating:

Opadry White 21S58740 (Hypromellose (E464), Ethylcellulose, Diethyl Phthalate, Titanium Dioxide (E171))

6.2 Incompatibilities

Chlorpromazine can increase the central nervous system depression produced by other CNS-depressant drugs including alcohol, hypnotics, sedatives or strong analgesics.

It antagonises the action of adrenaline and other sympathomimetic agents and reverses the blood pressure lowering effects of adrenergic blocking agents such as guanethidine and clonidine. It may impair the metabolism of tricyclic antidepressants, the anti-Parkinson effects of levodopa and the effects of anticonvulsants; it may possibly affect the control of diabetes, or the action of anticoagulants. Antacids can impair absorption. Tea and coffee may prevent absorption by causing insoluble precipitates.

Undesirable anticholinergic effects can be enhanced by anti-Parkinson or other anticholinergic drugs. It may enhance the cardiac-depressant effects of quinidine, the absorption of corticosteroids and digoxin, the effect of diazoxide and of neuromuscular blocking agents. Interactions with propranolol have been reported. The possibility of interaction with lithium should be borne in mind.

Further information: Chlorpromazine is a phenothiazine with an aliphatic side-chain. Its pharmacological profile of activity includes pronounced sedative and hypotensive properties, with fairly marked anticholinergic and anti-emetic activity and a moderate tendency to cause extrapyramidal reactions.

6.3 Shelf life

For Container pack: 36 months.

For Blister pack: 48 months

6.4 Special precautions for storage

Store below 25°C in a dry place, protect from light, keep containers closed.

6.5 Nature and contents of container

High density polystyrene with polythene lids and/or polypropylene containers with polypropylene or polythene lids and polyurethane/polythene wads.

PVC/aluminium foil blister packs.

Pack sizes: 28, 30, 50 56, 60, 84,100, 250, 500, 1000, 5000

250 micron PVC glass-clear/green rigid PVC (pharmaceutical grade). 20 micron hard-tempered aluminium foil coated on the dull side with 6-7 gsm heat seal lacquer and printed on the bright side.

Pack sizes: 28, 30, 50 56, 60, 84,100, 250, 500, 1000, 5000

6.6 Special precautions for disposal

No special instructions.

7 MARKETING AUTHORISATION HOLDER

Hualan Pharmaceuticals Limited
16/17 College Green
Dublin
D02 V078
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8 MARKETING AUTHORISATION NUMBER(S)

PL 52104/0018

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10 DATE OF REVISION OF THE TEXT

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