SUMMARY OF PRODUCT CHARACTERISTICS.

1. Name of the medicinal product

Chlorpromazine 100mg Tablets.

2. Qualitative and quantitative composition

Each tablet contains chlorpromazine hydrochloride 100mg and list of excipients provided in section 6.1

3. Pharmaceutical form

Film Coated Tablet

White, circular, biconvex, film coated tablets plain on both sides, packed in blister packs of 10 x10's contained in a unit box and in 1000's HDPE plastic container with literature insert.

4. Clinical particulars

4.1 Therapeutic indication

Chlorpromazine as a tranquilizer is used in the management of psychotic conditions e.g. schizophrenia and anxiety as an antiemetic, it is used to control nausea and vomiting of a variety of diseases and also those caused by various drugs plus post –operative nausea and vomiting. As an adjunct in the treatment of tetanus and cholera where in the latter chlorpromazine reduces the frequency and duration of diarrhea. Frequency of vomiting and the mean requirement for intravenous fluids. Chlorpromazine will be effective in alleviation of intractable hiccups and treatment of hypertensive emergencies.

4.2 Dosage and Administration

Chlorpromazine tablets are administered by the oral route.

Dose:

Adults: Chlorpromazine tablets are administered at a dose of 25 to 50 mg of the chlorpromazine hydrochloride three times daily and increasing as necessary. Daily doses of 75mg may be given as a single dose at night although psychotic patients may require up to 1g or more. Lower doses of 10 to 25mg may be sometimes required every 4-6 hours for the control of nausea and vomiting.

Children: 0.5mg per kg body weight every 4-6 hours by mouth for psychiatric conditions and children aged over 5 years is usually one-third to one-half the adult dose. Daily doses should not normally exceed 40mg for children aged 1 to 5 years or 75mg for children over 5 years of age.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Risk of angle-closure glaucoma.
- Risk of urinary retention related to urethroprostatic disorders.
- History of agranulocytosis
- Dopaminergic antiparkinsonism agents
- Chlorpromazine is contraindicated in cases of coma due to direct central nervous system depressants such as alcohol, barbiturates and opiates.
- Use in patients on concurrent therapy with other drugs potentially hemotoxic.
- Use in nursing mothers
- Gluten allergy or intolerance
- Citalopram, escitalopram

4.4 Precautions, warnings and side-effects:

1. The patient should be advised to avoid alcohol and not drive a vehicle or operate machinery during the first fell days of the treatment.
2. Avoid using concurrently, desferrioxamine, piperazine, tricyclic antidepressants and antiparkinsonism agents.
3. Adverse effects include antimuscarinic effects e.g. hypotension, extrapyramidal disorders, disturbance of endocrine and sexual functions. Skin reactions including photosensitivity may occur and some extent of sedation at the beginning of treatment.

4.5 Interactions with other medicinal products and other forms of interaction

Care should be exercised when giving Chlorpromazine to patients receiving**:**

Combinations contraindicated

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

Combinations not recommended

Dopaminergic antiparkinsonism agents (amantadine, bromocriptine, cabergoline, levodopa, lisuride, pergolide, piribedil, ropinirole) are not recommended: reciprocal antagonism of the antiparkinsonism agent and neuroleptic. 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. The drug may antagonise the effects of anti-Parkinson drugs, drugs causing electrolyte imbalance and metabolic inhibitors (CYP…) where known. QT prolonging drugs: there is an increased risk of arrhythmias when chlorpromazine is used with concomitant QT prolonging drugs (including certain antiarrhythmic and other antipsychotics including sultopride) and drugs causing electrolyte imbalance.

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 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

Combinations requiring precautions

Antidiabetic agents: concomitant administration of high chlorpromazine doses (100 mg/day), and antidiabetic agents can lead to an increase in blood sugar levels (decreased insulin release). Forewarn the patient and advise increased self-monitoring of blood and urine levels. If necessary, adjust the antidiabetic dosage during and after discontinuing neuroleptic treatment. Topical gastrointestinal agents (magnesium, aluminum 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). Atropine and other atropine derivatives: imipramine antidepressants, histamine H1-receptor antagonists, anticholinergic antiparkinsonism agents, atropinic antispasmodics, disopyramide: buildup of atropine-associated adverse effects such as urinary retention, constipation and dry mouth. Other CNS depressants: morphine derivatives (analgesics, antitussives and substitution treatments), barbiturates, benzodiazepines, anxiolytics other than benzodiazepines, hypnotics, sedative antidepressants, histamine H1 receptor antagonists, central antihypertensive agents increased central depression. Changes in alertness can make it dangerous to drive or operate machinery.

The concomitant administration of this product with other medications such as central nervous system depressants (including alcohol and anesthetics) or anti-hypertensives or anti-cholinergic will result in accentuation of their effects, while potentiation of action will also occur with monoamine oxidase inhibitors, anti-depressants and analgesics. Simultaneous administration of desferrioxamine and prochlorperazine has been observed to induce a transient metabolic encephalopathy characterized by loss of consciousness for 48 – 72 hours. This may occur with Chlorpromazine since it shares many of the pharmacological activities of prochlorperazine. Since chlorpromazine may cause hyperglycaemia or impair glucose tolerance the dose of oral hypoglycaemic or of insulin may need to be increased in diabetics.

4.6 Fertility, Pregnancy and lactation

Pregnancy: A large amount of exposure to chlorpromazine during pregnancy did not reveal any teratogenic effect. It is advised to keep an adequate maternal psychic balance during pregnancy in order to avoid decomposition. If a treatment is necessary to ensure this balance, the treatment should be started to continued ate effective dose all through 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, or feeding disorder. Consequently, newborns should be monitored carefully.

Lactation: Chlorpromazine is excreted in breast milk and use in nursing mothers is contraindicated.

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 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.
Adverse reactions listed below are classified according to frequency and system organ class. Frequency groupings are defined according to the following convention: very common (≥1/10), common (≥1/100to<1/10), uncommon (≥1/1,000to<1/100), rare (≥1/10,000to<1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Blood and lymphatic system disorders:
Not known: Agranulocytosis, Leukopenia

Immune system disorders
Not known: Systemic lupus erythematosus, antinuclear antibody positive

Endocrine disorders
Common: Hyperprolactinaemia, Amenorrhoea
Not known: Galactorrhoea, gynaecomastia, erectile dysfunction, Female sexual arousal disorder, impotence, and frigidity.

Metabolism and nutrition disorders
Very Common: Weight increased
Common: Glucose tolerance impaired
Not known: Hyperglycaemia, Hypertriglyceridemia, Hyponatremia, Inappropriate antidiuretic hormone secretion

Psychiatric disorders
Very Common: Anxiety
Not known: Lethargy, Mood altered

Nervous system disorders
Very common: Sedation, Somnolence, Dyskinesia, Tardive dyskinesia[3], Extrapyramidal disorder, Akathisia
Common: Hypertonia, Convulsion
Not known: Torticollis, Oculogyric crisis, Trismus, Akinesia, Hyperkinesia, Neuroleptic malignant syndrome
Use of phenothiazines at high (relative or absolute) doses may induce extrapyramidal side-effects, dyskinesia may develop in some patients on long term therapy, possibly in relation to total cumulative dose, or may develop after drug therapy have been discontinued. The risk is reported to be greater in elderly patients on high dose therapy. Characteristic symptoms rhythmical involuntary movements of the tongue, face, mouth or jaw sometimes accompanied by involuntary movements of the extremities. They persist for many months or even years and, while they gradually disappear in some patients, they appear to be permanent in others. At first signs of tardive dyskinesia which may be orofacial dyskinesia the benefit of continued treatment should be carefully assessed against the risk of development of persistent dyskinesia. Withdrawal of treatment with careful observation of the dyskinesia and psychotic condition has been suggested in order to assess the need for continued neuroleptic therapy and to reveal persisting dyskinesia. Should it be necessary to reinstate treatment, the antipsychotic agent may mask the syndrome. Antiparkinsonian agents have proved of little value in this syndrome.

Eye disorders
Not known: Accommodation disorder, Deposit eye

Cardiac disorders
Common: Electrocardiogram QT prolonged
Not known: Ventricular arrhythmia, Ventricular fibrillation, Ventricular tachycardia, Torsade de pointes, Cardiac arrest, Sudden death / sudden cardiac death (with possible causes of cardiac origin as well as cases of unexplained sudden death, in patients receiving neuroleptic phenothiazines)

Vascular disorders
Very common: Orthostatic or Postural hypotension.
Not known: Embolism venous, Pulmonary embolism (sometimes fatal), Deep vein thrombosis

Gastrointestinal disorders
Very common: Dry mouth, Constipation
Not known: Colitis ischemic Ileus paralytic Intestinal perforation (sometimes fatal), Gastrointestinal necrosis (sometimes fatal), Necrotizing colitis (sometimes fatal), Intestinal obstruction.

Hepatobiliary disorders
Not known: Jaundice cholestatic, liver injury, Cholestatic liver injury, mixed liver injury

Skin and subcutaneous tissue disorders

Not known: Dermatitis allergic, Angioedema, Urticaria, rash, Photosensitivity reaction
Renal and urinary disorders
Not known: Urinary retention (linked to anticholinergic effects)
Pregnancy, puerperium and perinatal conditions
Not known: Drug withdrawal syndrome neonatal
Reproductive system and breast disorders
Not known: Priapism
General disorders and administration site conditions
Not known: Temperature regulation disorder may be seen without evidence of clinical disease particularly at the start of treatment particularly during long term treatment; may occur after the neuroleptic is withdrawn and resolve after reintroduction of treatment or if the dose is increased in the anterior segment of the eye caused by accumulation of the drug but generally without any impact on sight.

4.9 Overdose.
Parkinsonism, convulsions, coma. Symptomatic treatment, continuous respiratory and cardiac monitoring (risk of prolonged QT interval) until the patient's condition resolves. Symptoms of chlorpromazine over dosage include drowsiness or loss of consciousness, hypotension, tachycardia, E.C.G. changes, ventricular arrhythmias and hypothermia. Severe extra-pyramidal dyskinesias may occur. 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. Generalized vasodilatation may result in circulatory collapse; raising the patient’s legs may suffice, in severe cases, volume expansion by intravenous fluids may be needed; infusion 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. Peripheral vasoconstrictor agents are not generally recommended; 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 must be considered. Avoid lignocaine, 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. Pharmacological properties.
5.1 Pharmacodynamics properties.
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-puritic, 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 vasodilatation, hypotension and tachycardia. Salivary and gastric secretions are reduced.

5.2 Pharmacokinetic properties.
Chlorpromazine is readily 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 proteins.

5.3 Preclinical safety data.
No additional data of relevance to prescriber.

6. Pharmaceutical particulars.

6.1 List of Excipients.

- Microcrystalline Cellulose pH 101 BP
- Pregelatinized Starch BP
- Sodium Starch Glycolate BP
- Povidone K-30 BP
- White corn starch (for paste) BP
- Purified Water BP
- Sodium Lauryl Sulphate BP
- Aerosil 200 Pharma BP
- Purified Talc BP
- Magnesium Stearate BP
- Hydroxypropyl Methylcellulose (5CPS) BP
- Ethyl Cellulose BP
- Titanium Dioxide BP
- Diethyl Phthalate BP
- Isopropyl Alcohol BP
- Methylene Chloride BP

6.2 Incompatibilities

None known

6.3 Shelf life

24 Months.

6.4 Special precautions for storage

Store in a dry place below 30ºC, Protect from light.
Keep all medicine out of reach of children.

6.5 Nature and contents of container

Packed in blister packs of 10 x10's contained in a unit box and in 1000's HDPE plastic container with literature insert.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

Marketing Authorization Holder:

Company Name: LABORATORY & ALLIED LTD.
Address: Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road,
P.O. Box 42875 GPO 00100, Nairobi.
Country : Kenya.
Telephone : +254 20 8040306.
Telefax : +254 20 8040309.
E-Mail : info@laballied.com.

Manufacturing Site Address:

Company Name: LABORATORY & ALLIED LTD.
Address: Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road,
P.O. Box 42875 GPO 00100, Nairobi.
Country : Kenya
Telephone : +254 20 8040306.
Telefax : +254 20 8040309.
E-Mail : info@laballied.com.

8. Marketing authorization number(s)

Kenya: Registration No. **H97/008.**

9. Date of first authorization/renewal of the authorization.
Date of first authorization in Kenya: 16/1/1997.
Retained: Annually.

10. Date of revision of the text.
March 2024.