1.4 PRODUCT INFORMATION.

1.4.1 Prescribing Information (Summary of Product Characteristics): *(Enclosed).*

1. Name of the medicinal product

Melasil Tablets.

2. Qualitative and quantitative composition

Each tablet contains: Metoclopramide Hydrochloride BP 5.0mg.
Each tablet contains: Lactose Monohydrate BP 58.52mg.
For more information on excipients see section 6.1

3.0 Pharmaceutical form: Tablet for oral administration.

White, circular, FFBE tablet, with a breakline on one side and plain on reverse side, packed in Alu/PVC blister packs of 10 x 10's contained in a unit box and bulk packs of 1000's in HDPE containers along with literature inserts.

4.0 Clinical particulars

4.1 Therapeutic indications

Melasil® (Metoclopramide) tablets are indicated in: -

- Radiological exploration of the gastrointestinal tract.
- Nausea, vomiting or Hiccups of digestive, peritoneal or neurological origin and post operative vomiting.
- For gastro-oesophageal reflux or gastric statis.
- Paediatrics-nausea and vomiting of any origin and gastric intolerance to drugs.

4.2 Posology and method of administration:

Method of administration: Oral administration.

Adults Patients:

Melasil® Tablets: Orally one tablet three times a day before food.
Melasil® Syrup: Orally 2 teaspoonfuls three times a day before food.

Children:

Age less than 1 year: 1mL twice daily.
One to three years: 1mL to three times daily.
Three to five years: 2mL two to three times daily.
Five to nine years: 2.5mL three times daily.
Nine to fourteen years: 5mL three times daily.
Fifteen to nineteen years: 5mg to 10mg 3 times daily depending upon body weight.
Higher doses have been used in cancer chemotherapy for controlling vomiting and nausea but should not exceed 10mg per kg body weight over 24 hours.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Gastrointestinal haemorrhage, mechanical obstruction or gastro-intestinal perforation for which the stimulation of gastrointestinal motility constitutes a risk.
- Confirmed or suspected pheochromocytoma, due to the risk of severe hypertension episodes.
- History of neuroleptic or metoclopramide-induced tardive dyskinesia.
- Epilepsy (increased crises frequency and intensity).
- Parkinson's disease.
- Combination with levodopa or dopaminergic agonists.
- Known history of methaemoglobinaemia with metoclopramide or of NADH cytochrome-b5 deficiency.
- Use in children less than 1 year of age due to an increased risk of extrapyramidal disorders.
- Melasil® should not be used during the first three to four days following operations such as pyloroplasty or gut anastomosis as vigorous muscular contractions may not help healing.

4.4 Special warnings and precautions for use

Precautions:

If vomiting persists the patient should be reassessed to exclude the possibility of an underlying disorder e.g. cerebral irritation.

Neurological Disorders:

Extrapyramidal disorders may occur, particularly in children and young adults, and/or when high doses are used. These reactions occur usually at the beginning of the treatment and can occur after a single administration. Metoclopramide should be discontinued immediately in the event of extrapyramidal symptoms. These effects are generally completely reversible after treatment discontinuation but may require a symptomatic treatment (benzodiazepines in children and/or anticholinergic anti-Parkinsonian medicinal products in adults).

The time interval of at least 6 hours specified in the section 4.2 should be respected between each metoclopramide administration,

even in case of vomiting and rejection of the dose, in order to avoid overdose.
Prolonged treatment with metoclopramide may cause tardive dyskinesia, potentially irreversible, especially in the elderly. Treatment should not exceed 3 months because of the risk of tardive dyskinesia (see section 4.8). Treatment must be discontinued if clinical signs of tardive dyskinesia appear.
Neuroleptic malignant syndrome has been reported with metoclopramide in combination with neuroleptics as well as with metoclopramide monotherapy (see section 4.8). Metoclopramide should be discontinued immediately in the event of symptoms of neuroleptic malignant syndrome and appropriate treatment should be initiated.
Special care should be exercised in patients with underlying neurological conditions and in patients being treated with other centrally-acting drugs.
Symptoms of Parkinson's disease may also be exacerbated by metoclopramide.
Methaemoglobinemia:
Methemoglobinemia which could be related to NADH cytochrome b5 reductase deficiency has been reported. In such cases, metoclopramide should be immediately, and permanently discontinued and appropriate measures initiated (such as treatment with methylene blue).
Cardiac Disorders:
There have been reports of serious cardiovascular undesirable effects including cases of circulatory collapse, severe bradycardia, cardiac arrest and QT prolongation following administration of metoclopramide by injection, particularly via the intravenous route. Special care should be taken when administering metoclopramide, particularly via the intravenous route to the elderly population, to patients with cardiac conduction disturbances (including QT prolongation), patients with uncorrected electrolyte imbalance, bradycardia and those taking other drugs known to prolong QT interval. Intravenous doses should be administered as a slow bolus (at least over 3 minutes) in order to reduce the risk of adverse effects (e.g. hypotension, akathisia).
Renal and Hepatic Impairment:
In patients with renal impairment or with severe hepatic impairment, a dose reduction is recommended.
Metoclopramide may cause elevation of serum prolactin levels.
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency of glucose-galactose malabsorption should not take this medicine.
Care should be exercised when using Metoclopramide in patients with a history of atopy (including asthma) or porphyria.
Metoclopramide should not be used in the immediate post-operative period (up to 3-4 days) following pyloroplasty or gut anastomosis, as vigorous gastrointestinal contractions may adversely affect healing.
Special care should be taken when administering Metoclopramide intravenously to patients with “sick sinus syndrome” or other cardiac conduction disturbances.
There have been very rare reports of abnormalities of cardiac conduction with intravenous metoclopramide. Metoclopramide should be used with care with other drugs affecting cardiac conduction.

4.5 Interaction with other medicinal products and other forms of interaction
Contraindicated combination:
Levodopa or dopaminergic agonists and metoclopramide have a mutual antagonism.
Combination to be avoided:
Alcohol potentiates the sedative effect of metoclopramide.
Combination to be taken into account:
Due to the prokinetic effect of metoclopramide, the absorption of certain drugs may be modified.
Anticholinergics and morphine derivatives:
Anticholinergics and morphine derivatives may have both a mutual antagonism with metoclopramide on the digestive tract motility.
Central nervous system depressants (morphine derivatives, anxiolytics, sedative H1 antihistamines, sedative antidepressants, barbiturates, clonidine and related)
Sedative effects of Central Nervous System depressants and metoclopramide are potentiated.
Neuroleptics:
Metoclopramide may have an additive effect with other neuroleptics on the occurrence of extrapyramidal disorders.
Serotonergic drugs:
The use of metoclopramide with serotonergic drugs such as SSRIs may increase the risk of serotonin syndrome.
Digoxin:
Metoclopramide may decrease digoxin bioavailability. Careful monitoring of digoxin plasma concentration is required.
Cyclosporine:
Metoclopramide increases cyclosporine bioavailability (Cmax by 46% and exposure by 22%). Careful monitoring of cyclosporine plasma concentration is required. The clinical consequence is uncertain.
Mivacurium and suxamethonium:
Metoclopramide injection may prolong the duration of neuromuscular block (through inhibition of plasma cholinesterase).
Strong CYP2D6 inhibitors:
Metoclopramide exposure levels are increased when co-administered with strong CYP2D6 inhibitors such as fluoxetine and paroxetine. Although the clinical significance is uncertain, patients should be monitored for adverse reactions.
Metoclopramide may reduce plasma concentrations of atovaquone.

4.6. Pregnancy and lactation

Pregnancy:

A large amount of data on pregnant women (more than 1000 pregnancy outcomes) indicates no malformative nor feto/neonatal toxicity of Metoclopramide hydrochloride. Metoclopramide can be used during pregnancy if clinically needed. Due to pharmacological properties (as other neuroleptics), in case of metoclopramide administration at the end of pregnancy, extrapyramidal syndrome in newborn cannot be excluded.

Metoclopramide should be avoided at the end of pregnancy. If metoclopramide is used, neonatal monitoring should be undertaken.

Breast-feeding

Metoclopramide is excreted in breast milk at low level. Adverse reactions in the breast-fed baby cannot be excluded. Therefore, metoclopramide is not recommended during breastfeeding. Discontinuation of metoclopramide in breastfeeding women should be considered.

Fertility:

No data available.

4.7 Effects on ability to drive and use machines

Metoclopramide has moderate influence on the ability to drive and use machines. Metoclopramide may cause drowsiness, dizziness, dyskinesia and dystonias which could affect the vision and also interfere with the ability to drive and operate machinery.

4.8 Undesirable effects

Adverse reactions listed by System Organ Class. Frequencies are defined 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 (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reactions
Blood and lymphatic system disorders		
	Not known	Methaemoglobinaemia, which could be related to NADH cytochrome b5 reductase deficiency, particularly in neonates (see section 4.4); Sulfhaemoglobinaemia, mainly with concomitant administration of high doses of sulphur-releasing medicinal products
Immune system disorders		
	Uncommon	Hypersensitivity
	Not known	Anaphylactic reaction (including anaphylactic shock particularly with intravenous formulation.
Endocrine disorders*		
	Uncommon	Amenorrhoea, Hyperprolactinaemia.
	Rare	Galactorrhoea.
	Not known	Gynaecomastia.
Psychiatric disorders		
	Common	Depression
	Uncommon	Hallucination
	Rare	Confusional state.
Nervous system disorders		
	Very common	Somnolence.
	Common	Extrapyramidal disorders (particularly in children and young adults and/or when the recommended dose is exceeded, even following administration of a single dose of the drug) (see section 4.4), Parkinsonism, Akathisia.
	Uncommon	Dystonia (including visual disturbances and oculogyric crisis), Dyskinesia, Depressed level of consciousness.
	Rare	Convulsion especially in epileptic patients.
	Not known	Tardive dyskinesia which may be persistent, during or after prolonged treatment, particularly in elderly patients (see section 4.4), Neuroleptic malignant syndrome (see section 4.4).
Cardiac disorders		
	Uncommon	Bradycardia, particularly with intravenous formulation.
	Not known	Cardiac arrest, occurring shortly after injectable use, and which can be subsequent to bradycardia (see section 4.4); Atrioventricular block, Sinus arrest particularly with intravenous formulation; Electrocardiogram QT prolonged; Torsade de Pointes;
Vascular disorders		
	Common	Hypotension, particularly with intravenous formulation.

	Not known	Shock, syncope after injectable use, Acute hypertension in patients with phaeochromocytoma (see section 4.3) Transient increase in blood pressure
Gastrointestinal disorders		
	Common	Diarrhoea.
General disorders and administration site conditions		
	Common	Asthenia.

* Endocrine disorders during prolonged treatment in relation with hyperprolactinaemia (amenorrhoea, galactorrhoea, gynaecomastia).

The following reactions, sometimes associated, occur more frequently when high doses are used:

- Extrapyramidal symptoms: acute dystonia and dyskinesia, parkinsonian syndrome, akathisia, even following administration of a single dose of the medicinal product, particularly in children and young adults (see section 4.4).
- Drowsiness, decreased level of consciousness, confusion and hallucination.

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 recommended channels.

4.9 Overdose.

Symptoms:

Extrapyramidal disorders, drowsiness, decreased level of consciousness, confusion, hallucination, and cardio-respiratory arrest may occur.

Management:

In case of extrapyramidal symptoms related or not to overdose, the treatment is only symptomatic (benzodiazepines in children and/or anticholinergic anti-parkinsonian medicinal products in adults).

A symptomatic treatment and a continuous monitoring of the cardiovascular and respiratory functions should be carried out according to clinical status.

5. 0 Pharmacological Properties

5.1 Pharmacodynamic Properties.

Pharmacotherapeutic group: Agents stimulating gastro-intestinal motility, **ATC code*:* A03FA01.**

Mechanism of action:

The action of metoclopramide is closely associated with parasympathetic nervous control of the upper gastro-intestinal tract where it has the effect of encouraging normal peristaltic action. This provides for a fundamental approach to the control of those conditions where disturbed gastrointestinal motility is a common underlying factor.

5.2 Pharmacokinetic properties

Metoclopramide is metabolised in the liver and the predominant route of elimination of metoclopramide and its metabolites is via the kidney.

Renal impairment:

The clearance of metoclopramide is reduced by up to 70% in patients with severe renal impairment, while the plasma elimination half-life is increased (approximately 10 hours for a creatinine clearance of 10-50 mL/minute and 15 hours for a creatinine clearance <10 mL/minute).

Hepatic impairment:

In patients with cirrhosis of the liver, accumulation of metoclopramide has been observed, associated with a 50% reduction in plasma clearance.

5.3 Preclinical safety data

No additional data available.

6. Pharmaceutical Particulars

6.1 List of excipients

- White Corn Starch.
- Lactose Monohydrate.
- Povidone K-30.
- Sodium Benzoate.
- Purified water.

- Aerosil 200 Pharma.
- Sodium Starch Glycolate.
- Sodium Lauryl Sulphate.
- Purified Talc.
- Magnesium Stearate.

6.2 Incompatibilities
None known.

6.3 Shelf-life
36 months (3 years) from the date of manufacture.

6.4 Special precautions for storage
Store in a dry place, below 30°C. Protect from light. Keep all medicines out of reach of children.

6.5 Nature and contents of container
Alu/PVC blister packs of 10 x 10's in a unit box and bulk pack of 1000's in HDPE containers along with a 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.

6.7 Distribution Category
Prescription Only Medicine (POM).

7. Marketing authorization holder/Registrant.
Laboratory & Allied Limited
Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road
P.O Box 42875 GPO 00100, Nairobi –Kenya.

8. Manufacturer
Laboratory & Allied Limited
Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road
P.O.BOX 42875 GPO 00100, Nairobi –Kenya
Email: info@laballied.com

9. Marketing Authorisation Number(s)
Registration No(s).: Kenya: H82147.

Date of registration: Kenya: 12th November 1982.
Retention: Retained annually.

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

11. Dosimetry (If Applicable):
Not Applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE):
Not Applicable.