1. Name of the medicinal Product

Metoclopramide Injection BP 10 mg/2 ml

2. Qualitative and Quantitative Composition

Each 2 ml contains metoclopramide hydrochloride BP equivalent to 10 mg of anhydrous metoclopramide hydrochloride

3. Pharmaceutical Form

Solution for Injection

A clear colorless solution.

4. Clinical Particulars

4.1 Therapeutic Indications Adults (20 years and over):

As an adjunct to X-ray examination of the stomach and duodenum. To assist in intestinal intubation and control nausea and vomiting associated with the following conditions: intolerance to essential drugs possessing emetic properties, uraemia, radiation sickness, malignant disease, postoperative vomiting, and lab our infectious diseases. There is no clear benefit in motion sickness or other labyrinth disturbances.
I.M administration of Perilin injection facilitates the absorption of a range of drugs including the absorption of aspirin in people with migraine. Perilin injection may found useful in the management of gastric retention after gastric surgery. Perilin injection may be useful in the treatment of diabetic gastroparesis of mild to moderate severity. Once control of diabetes has been established by diet and/or insulin, Perilin injection should be avoided.

Young adults and children over 1 year of age: The use of Perilin injection in patients under 20 years should be restricted to the following situations and only used as second line therapy:
Severe intractable vomiting of known cause.

Vomiting associated with radiotherapy and intolerance to cytotoxic drugs. As an aid to gastrointestinal intubation.

4.2 Posology and Method of Administration

Route of administration: *IM or by slow IV* injection (*1 to 2 minutes)*

Patients with normal renal and hepatic function: The dosage recommendations given below should be strictly adhered to if side effects of the dystonic type are to be avoided.
Total daily dosage of perilin injection, especially for children and young adults should not normally exceed 0.5 mg/kg bodyweight with a maximum of 30 mg daily. Perilin injection should only be used after careful examination to avoid masking an underlying disorder, e.g., cerebral irritation. Maximum recommended treatment duration is 5 days in all age groups.
Adults 20 years and over: Maximum of 10 mg three times a day. 1 to 3 times daily, I.V. or I.M. depending on the severity of the condition.

Elderly patients: To avoid adverse reactions strict adherence to dosage recommendations is advised and, where prolonged therapy is considered necessary, patients should be regularly reviewed.
Young adults and children over 1 year of age: Treatment of children should commence at the lower dosage, where stated, and used as second line therapy only.
Young adults: *15-19 years:* Treatment of young adults should commence at the lower dosage, and used as second line therapy only.5 mg to 10 mg three times a day.
Children 5 - 14 years: 2.5 mg to 5 mg (0.5 mL to 1 mL) two or three times daily.

3-5 years: 2 mg two or three times daily.

Children 1 - 3 years: 1.0 mg two or three times daily.

Diagnostic indications: A single dose of may be given 5 to 10 minutes before the examination.
Subject to bodyweight considerations, the following dosages are recommended:

Adults: 20 years and over: 10 to 20 mg

Young adults: 15-19 years: 10 mg

Children: *9-14 years:* 5 mg, *5-9 years:* 2.5 mg, 3-*5 years:* 2 mg, 1-*3 years:* 1 mg. **Patients with impaired renal and hepatic function:** In patients with clinically significant degrees of renal or hepatic impairment, clearance of Perilin injection is likely to be reduced. It is suggested that therapy be initiated at half the recommended dose. Subsequent dosage will depend on individual clinical response.

4.3 Contraindications

It should not be used whenever stimulation of gastrointestinal motility might be dangerous, e.g., in the presence of gastrointestinal hemorrhage, mechanical obstruction, or perforation.
It is contraindicated in patients with pheochromocytoma because the drug may cause a hypertensive crisis, probably due to release of catecholamines from the tumor. Such hypertensive crises may be controlled by phentolamine. It is contraindicated in patients with known hypersensitivity or intolerance to the drug. Porphyria. It may increase the frequency and severity of epilepsy (as seizures).It should not be administered to patients receiving other drugs which are likely to cause extrapyramidal reactions, since the frequency and severity of extrapyramidal reactions may be increased.

4.4 Special Warnings and Special Precautions for Use

Intravenous administration of perilin injection should be give slowly over a 1 to 2 minute period, since a transient but intense feeling of anxiety and restlessness, followed by drowsiness, may occur with rapid administration.
Persistent tardive dyskinesia: Treatment with Perilin injection can cause tardive dyskinesia (TD), a potentially irreversible and disfiguring disorder characterized by involuntary movements of the face, tongue, or extremities. Treatment with Perilin injection for longer than the recommended 12 weeks should be avoided in all but rare cases where therapeutic benefit is thought to outweigh the risk of developing TD. Perilin injection should be discontinued in patients who develop signs or symptoms of TD. There is no known effective treatment for established cases of TD. Therefore, perilin injection should not be used for the symptomatic control of TD. Extrapyramidal Symptoms (EPS) may occur with both perilin injection and neuroleptics such as phenothiazines, care should be taken in the event of both drugs being prescribed concurrently. Perilin injection given to epileptic patients the frequency and severity of seizures or extrapyramidal reactions may be increased.
Acute dystonic reactions occur in approximately 1% of patients given perilin injection. These occur more frequently in children and young adults and may occur after a single dose.
Perilin injection monotherapy may report neuroleptic malignant syndrome, combination with neuroleptics. Symptoms: hyperpyrexia, altered consciousness, muscle rigidity, autonomic instability and elevated levels of CPK and must be treated urgently (recognised treatments include dantrolene and bromocriptine). The treatment should be avoid immediately if this syndrome occurs.
Prolactin levels: Perilin injection elevates prolactin levels and the elevation persists during chronic administration. A factor of potential importance if the prescription of metoclopramide is contemplated in a patient with previously detected breast cancer.

Although disturbances such as galactorrhoea, amenorrhoea, gynaecomastia, and impotence may be reported with prolactin elevating drugs.
Other: Perilin Injection used (in such operation, pyloroplasty or gut anastomosis) should be withheld for three or four days as vigorous muscular contractions may not help healing.
The symptomatic relief provided by perilin may delay recognition of serious disease. It should not be prescribed until diagnosis has been established and should not be substituted for appropriate investigation of the patient's symptoms.
If vomiting persists in a patient receiving perilin injection, the patient should be reassessed to exclude the possibility of an underlying disorder e.g. cerebral irritation. Perilin injection may induced depression in patients without a prior history of depression. It should be given to patients with a prior history of depression only if the expected benefits outweigh the potential risks.
Perilin injection should be used with caution in patients with hypertension as on (I.V)

administration may show to release catecholamines.
Elderly: to avoid adverse reactions adhere strictly to dosage recommendations and where prolonged therapy is considered necessary, patients should be regularly monitored.
Paediatric use: It is contraindicated in children less than 1 year of age thus it should not be used in this age group. Unless a clearly indication has been established for its use, because of the to avoid higher incidence of adverse reactions.
Pregnancy: No adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.
Lactation: Metoclopramide is excreted in human milk. Caution should be exercised when metoclopramide is administered to a nursing mother.

4.5 Interaction with other medicinal products and other forms of interaction

The effects of metoclopramide on gastrointestinal motility are antagonized by anticholinergic drugs and narcotic analgesics. Additive sedative effects can occur when metoclopramide is given with alcohol, sedatives, hypnotics, narcotics, or tranquilizers. Since metoclopramide accelerates abnormally slow gastric and small bowel peristaltic activity. The absorption of drugs from the small bowel may be accelerated (e.g. paracetamol, tetracycline, L-dopa), whereas absorption of drugs from the stomach may be diminished (e.g. digoxin).
Metoclopramide may cause extrapyramidal symptoms in some patients. Therefore, when metoclopramide is used concomitantly with other drugs that are likely to cause extrapyramidal reactions, (e.g., neuroleptics such as phenothiazines), caution should be taken. The decrease in gastric emptying time caused by metoclopramide may increase the bioavailability of cyclosporin. Monitoring of cyclosporin concentrations may be necessary. When metoclopramide is given concurrently with suxamethonium the recovery time is prolonged.
Metoclopramide influences the delivery of food to the intestine and thus, the rate of its absorption, the administration of metoclopramide may result in poor diabetic control in some patients. Therefore, adjustment in, or timing of, insulin dosage may be necessary in insulin controlled diabetics.
The finding that metoclopramide releases catecholamines in patients with essential hypertension Suggests that it should be used cautiously, if at all, in patients receiving monoamine oxidase inhibitors.

4.6 Fertility, Pregnancy and Lactation

Pregnancy: No adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.
Lactation: Metoclopramide is excreted in human milk. Caution should be exercised when metoclopramide is administered to a nursing mother.

4.7 Effects on ability To Drive and use Machines

Patients should be cautioned about engaging in activities requiring mental alertness for a few hours after the drug has been administered.

4.8 Undesirable Effects

Less frequently, insomnia, headache, dizziness, nausea, or bowel disturbances may occur. Rarely may occur of acute depression. Anxiety or agitation also may occur, especially after rapid injection.
A single instance of supraventricular tachycardia following (IM) administration may be report. There may very rare of abnormalities of cardiac conduction (such as bradycardia and heart block) in association with intravenous metoclopramide. Atrial fibrillation, oedema, tachycardia and palpitations may be associated with the use of metoclopramide.
Extrapyramidal Reactions, Symptoms include, spasm of the facial muscles, trismus, rhythmic protrusion of the tongue, a bulbar type of speech, spasm of the extra ocular muscles including oculogyric crises, unnatural positioning of the head and shoulders and opisthotonos. There may be a generalised increase in muscle tone. The majority of reactions occur within 36 hours of starting treatment and the effects usually disappear within 24 hours of withdrawal of the drug, an antiparkinson drug such as benztropine or an anticholinergic antihistamine such as diphenhydramine should be given. A fatal dystonic reaction may report in a patient who received

hexamethylmelamine, cisplatin and high dose metoclopramide. A fatal cardiorespiratory arrest may occur in at least one patient with an acute dystonic reaction.
Tardive dyskinesia, which may be persistent, may report particularly in elderly patients undergoing long-term therapy with perilin injection.
Neuroleptic Malignant Syndrome: Very rare cases occurrences of this syndrome is potentially fatal and comprises hyperpyrexia, altered consciousness, muscle rigidity, autonomic instability and elevated levels of CPK and must be treated urgently (recognised treatments include dantrolene and bromocriptine). The treatment should be avoid immediately if this syndrome occurs.
Parkinsonian symptoms, including tremor, rigidity, bradykinesia and akinesia, occur rarely in patients Treatment with metoclopramide but may be associated with usual or excessive doses or with decreased renal function.
There may causes of hypersensitivity reactions such as urticaria, maculopapular rash.

A limited case of neutropenia, leucopenia, Sulfhaemoglobinaemia (in adults), methaemoglobinaemia may also report and agranulocytosis generally without perfect association with metoclopramide.
Galactorrhoea and breast enlargement, raised serum prolactin levels.

Respiratory failure, secondary to dystonic reaction, acute asthmatic symptoms of wheezing and dyspnoea may occur. Urinary incontinence and frequency, sexual dysfunction, priapism and muscle spasm may also occur. Rarely, cases of hepatotoxicity, characterized by such as jaundice and altered liver function tests, when metoclopramide taken with other drugs with known hepatotoxic potential.

4.9 Overdose

Symptoms: The overdose of metoclopramide can rise, Drowsiness, disorientation and extrapyramidal, precise hardly AV block, feelings of anxiety or restlessness, headache, vertigo, nausea, vomiting, constipation, weakness, hypotension and xerostomia.
Treatment**:** The overdosage of metoclopramide symptomatic and supportive therapy may be followed. Antiparkinson and antihistamine/anticholinergic drugs such as diphenhydramine hydrochloride have effectively controlled extrapyramidal reactions. Haemodialysis appears ineffective in removing metoclopramide. Similarly, continuous ambulatory peritoneal dialysis does not remove significant amounts of the drug.

5. Pharmacological Properties

5.1 Pharmacodynamics Properties

Metoclopramide has antiemetic, antinauseant and gastrokinetic activity. It stimulates motility of the upper gastrointestinal tract without stimulating gastric, biliary or pancreatic secretions. The rate of gastric emptying is increased due to increased peristalsis of the jejunum and duodenum. The tone and amplitude of gastric contractions are increased, with relaxation of the pyloric sphincter and duodenal bulb. These effects combine to result in decreased intestinal transit time. The effect of metoclopramide on motility is not dependent on intact vagal innervation, but it can be abolished by anticholinergic drugs. Metoclopramide has little, if any, effect on the motility of the colon or bladder. Metoclopramide also exhibits dopamine antagonist activity and consequently produces sedation and, rarely, other extrapyramidal reactions. It may have serotonin receptor (5HT3) antagonist properties. Metoclopramide inhibits the central and peripheral effects of apomorphine, induces release of prolactin and produces a transient increase in circulating aldosterone levels.

5.2 Pharmacokinetic Properties

Absorption: Following intravenous administration, the onset of action is within 1 to 3 minutes and after intramuscular administration, this interval is extended to 10 to 15 minutes. The effect usually lasts from 1 to 2 hours.
Protein Binding: Plasma protein binding is 13% to 22%.

Metabolism: About 80% of the drug is excreted in the urine in the first 24 hours after administration. Approximately half is unchanged metoclopramide and half is the glucuronide and sulphate conjugate.
Elimination: Metabolism mainly occurs in the liver and elimination half-life may vary from 2.5 to 6 hours. Impaired renal function results in a reduced clearance and an increased half-life, up to 15 hours. The drug is not extensively bound to plasma proteins. The whole body volume of distribution is high which suggests extensive distribution of drug to the tissues.

5.3 Preclinical Safety Data

No data available.

6. Pharmaceutical Particulars

6.1 List of Excipients

Sodium Chloride (Inj. Grade)

Citric acid monohydrate BP
Sodium Citrate BP
Water for Injections BP

6.2 Incompatibilities

If it is used for the treatment of nausea and vomiting associated with cytotoxic drugs, the cytotoxic agent should be administered as a separate infusion.

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Do not store above 30°C. Protect from light.

6.5 Nature and Contents of Container

2 ml clear glass ampoule (White ring, autocut),such 10 ampoules are packed in blister using “LPL” logo printed paper foil , such 1 blister is packed in printed carton along with packing insert.

6.6 Special precaution for disposal and other handling

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

7. Marketing Authorization Holder

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8. Marketing Authorization Number

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