Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Metoclopramide hydrochloride 5 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains metoclopramide hydrochloride monohydrate equivalent to 5 mg of metoclopramide hydrochloride.
Each ampoule of 2 ml contains metoclopramide hydrochloride monohydrate equivalent to 10 mg of metoclopramide hydrochloride.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection (Injection).

Clear, colourless, solution for injection.

pH: 3.0 – 5.0

Osmolarity 292 mOsm/L

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Adult population
Metoclopramide hydrochloride is indicated in adults for:

- Prevention of post operative nausea and vomiting (PONV)
- Symptomatic treatment of nausea and vomiting, including acute migraine induced nausea and vomiting
- Prevention of radiotherapy induced nausea and vomiting (RINV).

Paediatric population
Metoclopramide hydrochloride is indicated in children (aged 1 – 18 years) for:

- Prevention of delayed chemotherapy induced nausea and vomiting (CINV) as a second line option
- Treatment of established post operative nausea and vomiting (PONV) as a second line option.

4.2 Posology and method of administration

The solution can be administered intravenously or intramuscularly.
Intravenous doses should be administered as a slow bolus (at least over 3 minutes).

All indications (adult patients)
For prevention of PONV a single dose of 10 mg is recommended.
For the symptomatic treatment of nausea and vomiting, including acute migraine induced nausea and vomiting and for the prevention of radiotherapy induced nausea and vomiting (RINV): the recommended single dose is 10 mg, repeated up to three times daily.
The maximum recommended daily dose is 30 mg or 0.5 mg / kg body weight.
The injectable treatment duration should be as short as possible and transfer to oral or rectal treatment should be made as soon as possible.

All indications (paediatric patients aged 1 – 18 years)
The recommended dose is 0.1 to 0.15 mg / kg body weight, repeated up to three times daily by intravenous route. The maximum dose in 24 hours is 0.5 mg / kg body weight.

Dosing table

Age	Body Weight	Dose	Frequency
1 – 3 years	10 – 14 kg	1 mg	Up to 3 times daily
3 – 5 years	15 – 19 kg	2 mg	Up to 3 times daily
5 – 9 years	20 – 29 kg	2.5 mg	Up to 3 times daily
9 – 15 years	30 – 60 kg	5 mg	Up to 3 times daily
15 – 18 years	Over 60 kg	10 mg	Up to 3 times daily

The maximum treatment duration is 48 hours for treatment of established post operative nausea and vomiting (PONV).
The maximum treatment duration is 5 days for prevention of delayed chemotherapy induced nausea and vomiting (CINV).

Frequency of administration:
A minimal interval of 6 hours between two administrations is to be respected, even in case of vomiting or rejection of the dose (see section 4.4).

Special population

Elderly:
In elderly patients a dose reduction should be considered, based on renal and hepatic function and overall frailty.

Renal impairment:
In patients with end stage renal disease (Creatinine clearance < 15 ml / min), the daily dose should be reduced by 75 %.
In patients with moderate to severe renal impairment (Creatinine clearance 15 – 60 ml / min), the dose should be reduced by 50 % (see section 5.2).

Hepatic impairment:
In patients with severe hepatic impairment, the dose should be reduced by 50 % (see section 5.2).
Other pharmaceutical forms may be more appropriate for administration to this population.

Paediatric population:
Metoclopramide is contraindicated in children aged less than 1 year (see section 4.3).

Method and route of administration
The solution can be administered intravenously or intramuscularly.
Intravenous doses should be administered as a slow bolus (at least over 3 minutes).
Due to the potential risk of severe cardiovascular reactions including cardiac arrest, the solutions for injection are restricted to be used only when appropriate resuscitation equipment is available (see section 4.8).

4.3 Contraindications

This medicine SHOULD NOT BE USED in the following cases:

- 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 (see section 4.5).
- Known history of methaemoglobinaemia with metoclopramide or of NADH cytochrome-b5 deficiency.
- Prolactin-dependent tumors.
- Use in children less than 1 year of age due to an increased risk of extrapyramidal disorders (see section 4.4).

This medicine SHOULD NOT BE USED in combination with alcohol (see section 4.5 "Interaction with other medicinal products and other forms of interaction").

4.4 Special warnings and precautions for use

Warnings
Do not increase the doses beyond the recommended dose.

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 (see section 4.3).

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 (see section 4.8).
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 (see section 4.2).

Precautions
IV injections should be made slowly, at least over 3 minutes.

Atovaquone
Concomitant treatment with atovaquone is not recommended (see section 4.5).

Excipients with known effect:
This medicine contains less than 1 mmol sodium (23 mg) per ampoule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Contraindicated combination
Levodopa or dopaminergic agonists and metoclopramide have a mutual antagonism (see section 4.3).

Combination to be avoided
Alcohol potentiates the sedative effect of metoclopramide.

Atovaquone
Concomitant treatment with metoclopramide has been associated with a significant decrease (about 50 %) in plasma concentrations of atovaquone. The combination should be avoided (see section 4.4).

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 (C_{max} 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.

4.6 Fertility, pregnancy and lactation

Pregnancy
A large amount of data on pregnant women (more than 1000 exposed outcomes) indicates no malformative toxicity nor foetotoxicity. 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.

Breastfeeding
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.

4.7 Effects on 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).

Systeme 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
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; Blood pressure increase in patients with or without phaeochromocytoma (see section 4.3).
Endocrine disorders*		
	Uncommon	Amenorrhoea, Hyperprolactinaemia,
	Rare	Galactorrhoea
	Not known	Gynaecomastia
Gastrointestinal disorders		
	Common	Diarrhoea
General disorders and administration site conditions		
	Common	Asthenia
Immune system disorders		
	Uncommon	Hypersensitivity
	Not known	Anaphylactic reaction (including anaphylactic shock) particularly with intravenous formulation
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)
Psychiatric disorders		
	Common	Depression with light or severe symptoms including

		suicidal thoughts
	Uncommon	Hallucination
	Rare	Confusional state
	Not known	Suicidal ideation
Vascular disorder		
	Common:	Hypotension, particularly with intravenous formulation
	Not known	Shock, syncope after injectable use, Transient increase in blood pressure.

* 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, 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 the HPRA Pharmacovigilance Website: www.hpra.ie.

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 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for functional gastrointestinal disorders, Propulsives.
ATC code: A03FA01
Metoclopramide is a neuroleptic antagonist of dopamine. It prevents vomiting by blocking dopaminergic sites.

5.2 Pharmacokinetic properties

Distribution
Metoclopramide is vastly distributed in the tissue. The volume of distribution is 2.2 to 3.4 L / kg. Metoclopramide shows little attachment to plasma proteins. It passes through the placenta and in breast milk.

Biotransformation
Metoclopramide is poorly metabolized.

Elimination
Primarily eliminated in urine, in free form or as sulfate conjugates. The elimination half-life is 5 to 6 hours. This increases in the event of renal or hepatic insufficiency.

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

These data do not indicate the need for any further precautions for use other than those already described above.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium hydroxide *(for pH adjustment)*
Hydrochloric acid *(for pH adjustment)*
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

3 years

After admixture/dilution: Chemical and physical in-use stability of admixtures with sodium chloride 0.9 %, dextrose 5 %, Ringer's Lactate and 4 % dextrose in 0.18 % sodium chloride are stable for 48 hours at 15-25^{o}C under artificial light and for 48 hours at 5 (±3)^{o}C, at a concentration of Metoclopramide hydrochloride 0.1 mg / ml.
From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

After first opening:
Use within 2 months if the ampoules are stored without the pouch.

6.4 Special precautions for storage

Keep the ampoules in the pouch or in the commercial packaging (pouch and outer carton) in order to protect from light.

This medicinal product does not require any special temperature storage conditions.
For storage conditions after first opening and/or admixture/dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Polypropylene ampoules containing 2 ml of solution, packed in carton boxes of 5, 10 (2x5), 20 (4x5), 50 (10x5) or 60 (12x5) ampoules.
Each 5 ampoules are overwrapped with a protective pouch.

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.

Compatibility
Metoclopramide hydrochloride can be admixtured/diluted in sodium chloride 0.9 % solution, dextrose 5 %, Ringer's Lactate solution and 4 % dextrose in 0.18 % sodium chloride, at a final concentration of Metoclopramide hydrochloride 0.1 mg / ml.

7 MARKETING AUTHORISATION HOLDER

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Mitsi Building 3, Office 115
1065 Nicosia
Cyprus

8 MARKETING AUTHORISATION NUMBER

PA1122/042/001

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May 2026