SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Metoclopramide 10 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains metoclopramide hydrochloride 10.50 mg equivalent to 10mg of the anhydrous substance.

Excipients with known effect: lactose and sodium.
Each tablet contains 80 mg lactose.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

White normal convex tablets engraved with the company logo on one side and scored on the other, engraved with “A” above and “306” below the score.

4.1 Therapeutic indications

Adult population

Metoclopramide is indicated in adults for:

-Prevention of delayed chemotherapy induced nausea and vomiting (CINV).
-Prevention of radiotherapy induced nausea and vomiting (RINV).
-Symptomatic treatment of nausea and vomiting, including acute migraine induced nausea and vomiting. Metoclopramide can be used in combination with oral analgesics to improve the absorption of analgesics in acute migraine.

Diagnostic procedures:
Radiology,
Duodenal intubation

Metoclopramide speeds up the passage of a barium meal by increasing the rate of
gastric emptying, co-ordinating peristalsis and dilating the duodenal bulb.
Metoclopramide also facilitates duodenal intubation procedures

Paediatric population

Metoclopramide is indicated in children (aged 1 to 18 years) for:
Prevention of delayed chemotherapy induced nausea and vomiting (CINV) as

a second line option.

4.2 Posology and method of administration

Posology

Adult patients

The recommended single dose is 10 mg, repeated up to three times daily.

The maximum recommended daily dose is 30 mg or 0.5mg/kg body weight.

The maximum recommended treatment duration is 5 days.

Paediatric population

The safety and efficacy of metoclopramide in children below 1 year has not yet been established (see section 4.3).

Prevention of delayed chemotherapy induced nausea and vomiting (CINV) (paediatric patients aged 1 to 18 years)

The recommended dose is 0.1 to 0.15 mg/kg body weight, repeated up to three times daily by oral use. 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
9-18 years	30-60 kg	5 mg	Up to 3 times daily
15-18 years	Over 60kg	10 mg	Up to 3 times daily

The maximum treatment duration is 5 days for prevention of delayed chemotherapy induced nausea and vomiting (CINV).

Tablets are not suitable for use in children weighing less than 61 kg. Other pharmaceutical forms/strengths may be more appropriate for administration to this population.

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 populations

Elderly

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

Patients with *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).

Patients with *Hepatic impairment*

In patients with severe hepatic impairment, the dose should be reduced by 50% (see section 5.2).

Other pharmaceutical forms/strengths may be more appropriate for administration to the above populations.

Diagnostic indications:

A single dose of ' metoclopramide tablets ' may be given 5-10 minutes before the examination, subject to body weight consideration, (see above).

Method of administration : For oral use only

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 (see section 4.5).

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 (see section 4.4).

Metoclopramide 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 (see section 4.3)

Symptoms of Parkinson's disease may also be exacerbated by metoclopramide.

Methaemoglobinemia

Methaemoglobinemia 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 "sick sinus syndrome" or 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 reactions (*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).

Metoclopramide may cause elevation of serum prolactin levels.

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.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency of glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23mg) per tablet, 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.

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 both have 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 ciclosporin bioavailability (C_{max} by 46% and exposure by 22%). Careful monitoring of ciclosporin 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 Fertility, pregnancy and lactation

Pregnancy
A large amount of data on pregnant women (more than 1,000 pregnancy outcomes) indicates no malformative nor feto/neonatal toxicity. 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 new-born 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
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 disorder		
	Common	Hypotension, particularly with intravenous formulation
	Not known	Shock, syncope after injectable use, Acute hypertension in patients with pheochromocytoma (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, 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 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

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.

SUMMARY OF PRODUCT CHARACTERISTICS

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Agents stimulating gastro-intestinal motility, ATC Code A03F A01

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

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5.3 Preclinical safety data

No additional data available

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize starch
Pregelatinised starch
Magnesium stearate
Sodium starch glycollate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years for Opaque plastic containers

3 years for Blister packaging

6.4 Special precautions for storage

Store below 25˚C.

Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

Metoclopramide tablets are packed in the following containers and closures:
1. Opaque plastic containers made of polypropylene tubes and polyethylene caps for all pack sizes (28, 30, 42, 50, 56, 60, 84, 90, 100, 112, 250, 500 and 1000).
2. Opaque plastic container composed of either high density polypropylene or high density polyethylene with a tamper evident or child resistant tamper evident closure composed of high density polyethylene with a packing inclusion of standard polyether foam or polyethylene or polypropylene filler for all pack sizes (28, 30, 42, 50, 60, 84, 90, 100, 112, 250, 500 and 1000).
3. Blister packs of aluminium/opaque PVC. It is subsequently packed in printed boxboard cartons in pack sizes of 28, 30, 42, 56, 60, 84, 90 and 112.

6.6 Special precautions for disposal

No special instructions for use/handling.

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

7 MARKETING AUTHORISATION HOLDER

Crescent Pharma Limited, Key House,

Sarum Hill, Basingstoke, RG21 8SR,

United Kingdom.

8. MARKETING AUTHORISATION NUMBER

PL 20416/0103

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12 January 2004

10 DATE OF REVISION OF THE TEXT

23/05/2025