

SUMMARY OF PRODUCT CHARACTERISTICS

PRODUCT SUMMARY

1. NAME OF THE MEDICINAL PRODUCT

Metoclopramide 5 mg/ml Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Each 20 ml contains metoclopramide hydrochloride BP equivalent to 100 mg of anhydrous metoclopramide hydrochloride.

3. PHARMACEUTICAL FORM

Sterile injection or infusion.

4. Clinical Particulars

4.1 Therapeutic indications

Paediatric population including adolescents:

Metoclopramide is indicated for the treatment of postoperative nausea and vomiting for children from 1 year of age.

For other indications, the use in the paediatric population is not recommended.

Adult population:

1) The use of metoclopramide in young adult patients (16 to 19 years) should be restricted to the following: severe intractable vomiting of known cause, vomiting associated with radiotherapy and intolerance to cytotoxic drugs, as an aid to gastro-intestinal intubation, as part of the pre-medication before surgical procedures.

2) As a dopamine antagonist, motility stimulant to gastric emptying and small intestinal transit time by increasing gastric peristalsis and increasing the resting tone of the gastro-oesophageal sphincter.

3) Relief of symptoms associated with oesophageal reflux.

4) Treatment of non-specific or cytotoxic induced nausea and vomiting.

5) Relief of symptoms associated with migraine such as nausea and vomiting by speeding up gastric emptying. This also improves the absorption of concurrently administered analgesics such as paracetamol.

6) In diagnostic procedures, speeding transit time of radiopaque materials by increasing gastric emptying.

7) To facilitate intubation of the small intestine in patients in whom the tube (e.g. endoscope, biopsy tube) does not pass through the pylorus with conventional manoeuvres.

The 50 mg in 10 ml and 100 mg in 20 ml strength is deliberately formulated to provide for high dose therapy to counteract nausea and vomiting associated with cytotoxic therapy.

The 50 mg in 10 ml and 100 mg in 20 ml are not intended to be used for the broad indications outlined in the application for Metoclopramide 10 mg in 2 ml as reactions associated with metoclopramide are more likely with these higher doses.

4.2 Posology and method of administration

Paediatric population:

For the treatment of postoperative nausea and vomiting, metoclopramide should be administered after the termination of the surgical procedure.

The recommended dose in children aged 1-15 yrs old is 0.15 mg/kg b.w. given as a slow injection (at least 3 minutes).

The maximum dose in 24 hours is 0.5 mg/kg b.w. If additional doses are needed, these should be separated by at least 6 hours.

Metoclopramide should not be used in children younger than 1 year as there are insufficient data regarding efficacy and safety of the product in this patient population.

Adult population:

Metoclopramide 5 mg/ml Injection 10 mg in 2ml

Metoclopramide 5 mg/ml Injection 10 mg in 2ml should be given by intramuscular injection or by slow intravenous injection (over 2 minutes).

The potential for side effects such as dystonia is increased if the dosage exceeds that recommended below.

Each 2 ml of Metoclopramide 5 mg/ml Injection contains 10 mg of anhydrous substance.

For treatment and relief of symptoms numbering 1 – 5 (see section 4.1):

Adult patients (20 years and over):

60 kg and above	10 mg three times daily
below 60 kg	5 mg three times daily

Young adult patients (16 to 19 years):

Caution should be exercised when treating young adults. Dosage schedules should be calculated according to body weight and commenced at the lower dosage where stated.

Above 60 kg	As above
30 – 59 kg	5 mg three times daily

Doses should not exceed 0.5 mg per kg body weight as a total daily dose.

For diagnostic procedures numbers 6 and 7 (see section 4.1):

A single IV dose may be given 10 minutes before the investigation.

Above 60 kg	10 mg
30 – 59 kg	5 mg

Elderly patients dosage: As for adults. The recommended doses for adults should not be exceeded in the elderly. In particular during long term therapy in the elderly, dosage should be regularly reviewed.

Metoclopramide should be used with caution and in reduced dosage during prolonged therapy in patients with clinically significant degrees of renal or hepatic impairment. Metoclopramide is metabolised in the liver and the predominant route of elimination of metoclopramide and its metabolites is via the kidney.

Metoclopramide 5 mg/ml Injection 50 mg in 10 ml and 100 mg in 20 ml

Metoclopramide 5 mg/ml Injection 50 mg in 10 ml and 100 mg in 20 ml suitably diluted are infused intravenously over at least 15 minutes.

Metoclopramide Injection has been shown to be compatible with the following infusion solutions:

Sodium chloride Intravenous infusion BP (0.9% w/v)

Dextrose Intravenous Infusion BP (5% w/v)

Sodium chloride and Dextrose Intravenous Infusion BP (Sodium chloride 0.18% w/v and Dextrose 4% w/v)

Compound sodium lactate Intravenous Infusion BP (Ringer lactate solution, Hartman's solution)

Dosage

Adult patients (20 years and over):

Up to 2 mg/kg body weight by i.v. infusion in a suitable diluent 30 minutes before administration of a highly emetogenic drug and repeated twice at 2 hour intervals following the initial dose.

Doses of metoclopramide should not exceed 10 mg per kg body weight in 24 hours.

Metoclopramide can also be given by continuous infusion as a loading dose followed by continuous infusion:

Loading dose: 2 – 4 mg per kg body weight over 15 – 30 minutes
Maintenance dose: 3 – 5 mg per kg body weight over 8 – 12 hours
(maximum dose: 10 mg per kg body weight in 24 hours)

Elderly patients

Dose as for adults, but it is important to follow dosage recommendations and not to exceed them because of the increased risk of dystonic reactions and the possibility of varying degrees of renal dysfunction. Closely monitor patients if therapy is prolonged.

4.3 Contraindications

Metoclopramide is contraindicated in neonates.

Hypersensitivity to metoclopramide or any of the ingredients.

Metoclopramide should not be used where gastro intestinal conditions might be adversely affected, as in intestinal obstruction, perforation or haemorrhage or immediately after surgery.

Other underlying causes of vomiting such as cerebral irritation should be excluded as use of metoclopramide may mask such symptoms.

Metoclopramide should be avoided in patients with phaeochromocytoma as concurrent administration may precipitate hypertensive crises.

Metoclopramide should not be used during breast feeding (see 4.6).

4.4 Special warnings and precautions for use

Extrapyramidal disorders may occur, particularly in children and young adults and/or when high doses are used (see 4.8. undesirable effects).

Respect the time interval (at least 6 hours) specified for children in the dosage section between each metoclopramide administration, even in case of vomiting, in order to avoid overdose.

Metoclopramide should be used in caution in patients with hepatic and renal impairment and in the elderly, young adults and children. Special care should be taken in cases of severe renal and hepatic insufficiency (see also section 4.2 Posology and method of administration).

Metoclopramide should be used with caution in patients with hypertension, since there is limited evidence that the drug may increase circulating catecholamines in such patients. The frequency and severity of seizures may be increased by metoclopramide, in patients with a history of seizure disorders. Metoclopramide should only be given with great caution in patients receiving drugs that are likely to cause extrapyramidal reactions (e.g. phenothiazines, butyrophenones), since the frequency and severity of these reactions may be increased by metoclopramide especially in children / young adults.

The neuroleptic malignant syndrome has been reported with metoclopramide in combination with neuroleptics as well as with metoclopramide monotherapy (see section 4.8 Undesirable effects).

Metoclopramide should be used with care in combination with other serotonergic drugs including SSRIs (see section 4.5 Interactions).

Metoclopramide may mask symptoms underlying conditions such as cerebral irritation and pregnancy.

Care should be exercised when using metoclopramide in patients with a history of atopy (including asthma) or porphyria.

Care should be exercised in epileptic patients and patients being treated with other centrally acting drugs.

Because metoclopramide can stimulate gastro-intestinal mobility, the drug theoretically could produce increased pressure on the suture lines following gastro-intestinal anastomosis or closure.

4.5 Interactions with other medicinal products and other forms of interaction

Metoclopramide may affect the absorption of other drugs, either by diminishing absorption from the stomach or by enhancing the absorption from the small intestine (e.g. the effects of paracetamol and aspirin are enhanced). The effects of CNS depressants may be enhanced.

Metoclopramide may increase the absorption of ciclosporin and raise its blood levels

The action of metoclopramide on the gastro-intestinal tract is antagonised by anticholinergics and opioid analgesics.

Since metoclopramide may cause extrapyramidal reactions, care should be taken when using in combination with other drugs with similar effects (e.g. phenothiazines, butyrophenones, tetrabenazine) (see 4.4 Special warnings and precautions for use). The effects of anti-Parkinson agents such as levodopa, amantadine, pergolide and ropinirole may be reduced.

Metoclopramide may antagonise the hypoprolactinaemic effect of prolactin, and medications such as bromocriptine and cabergoline.

The use of metoclopramide with serotonergic drugs may increase the risk of serotonin syndrome.

Metoclopramide may reduce plasma concentrations of atovaquone.

Metoclopramide enhances the neuromuscular blocking effects of suxamethonium.

4.6 Pregnancy and lactation

Reproduction studies in animals have not revealed evidence of harm to the foetus. There are no adequate and controlled studies using metoclopramide in pregnant women, therefore, the drug should be used during pregnancy only when clearly needed and is not recommended in the first trimester.

Since metoclopramide is distributed into milk, the drug should not be used in nursing mothers.

4.7 Effects on ability to drive and use machines

Metoclopramide may cause side effects including drowsiness, dyskinesia, dystonias and visual disturbances which could interfere with the ability to drive or operate machinery (see also section 4.8 Undesirable effects).

4.8 Undesirable effects

Blood and lymphatic system disorders

Very rare cases of red cell disorders such as methaemoglobinaemia (which could be related to NADH cytochrome b5 reductase deficiency particularly in neonates) and sulphaemoglobinaemia have been reported, particularly at high doses of metoclopramide, and may be more severe in patients with G6PD deficiency. Metoclopramide should be withdrawn and appropriate treatment instituted.

Immune system disorders

Very rarely, hypersensitivity, including anaphylaxis, bronchospasm and cutaneous reactions, has been reported (see also Skin and subcutaneous tissue disorders)

Endocrine disorders

Raised prolactin levels, resulting in galactorrhoea, irregular menstrual periods and gynaecomastia may occur during metoclopramide therapy.

Psychiatric disorders

Rare cases of confusion, restlessness, anxiety and depression have been reported.

Nervous system disorders

Metoclopramide may cause extrapyramidal reactions such as acute dystonia and dyskinesia, parkinsonian syndrome, akathisia, even following administration of a single dose of the drug, particularly in children and young adults (see Section 4.4.). These reactions may occur following single or low dose regimes, but are more likely if the dose of metoclopramide is above 500 micrograms per kg body weight. Dystonic reactions 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. Extrapyramidal reactions generally occur within 24 – 48 hours of starting treatment, and the effects usually disappear within 24 hours of withdrawal of the drug.

Should treatment of a dystonic reaction be required, an anticholinergic anti-Parkinson drug, or a benzodiazepine may be used.

Chronic tardive dyskinesia, which may be irreversible, has developed in patients receiving long term therapy with metoclopramide. This occurs most commonly in geriatric patients (particularly women) and usually develops following discontinuation of the drug. It is manifested by orobuccolingual dyskinesic movements. Patients on prolonged therapy should be regularly reviewed. Very rare occurrences of neuroleptic malignant syndrome have been reported. This syndrome is potentially fatal and comprises

hyperpyrexia, altered consciousness, muscle rigidity, autonomic instability and elevated levels of creatine phosphokinase (CPK) and must be treated urgently (recognised treatments include dantrolene and bromocriptine). Metoclopramide should be stopped immediately if this syndrome occurs.

Drowsiness, fatigue and dizziness may occur (rare).

Cardiac disorders

Very rare reports of abnormalities of cardiac conduction (bradycardia, asystole, heart block) have been reported following intravenous administration.

Vascular disorders

Transient hypotension followed by compensatory tachycardia may occur.

Hypertensive crises have occurred in patients with phaeochromocytomas given metoclopramide.

Gastrointestinal disorders

Diarrhoea

Skin and subcutaneous tissue disorders

Skin reactions such as rash, pruritus, angioedema and urticaria.

General and Administration Site Disorders

Very rare reports of injection site inflammation and local phlebitis have been received

4.9 Overdose

Treatment of metoclopramide overdosage, generally involves symptomatic and supportive care. There is no specific antidote for metoclopramide; however, agents with central anticholinergic activity (e.g. diphenhydramine, benztropine) may be useful in extrapyramidal reactions (benzodiazepines in children). The patient should be treated with gastric lavage.

Symptoms of metoclopramide overdose are generally self-limiting and usually subside within 24 hours. Haemodialysis or peritoneal dialysis is unlikely to enhance the elimination of metoclopramide.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Metoclopramide as a dopamine antagonist stimulates gastric motility and gastric emptying and speeds small intestinal transit time by increasing gastric peristalsis and increasing the resting tone of the gastro oesophageal sphincter.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

No further information other than that which is included in the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride
Citric Acid Monohydrate
Sodium Citrate
Water for Injections
Hydrochloric acid
Sodium hydroxide
Nitrogen

6.2 Incompatibilities

Any dilutions of Metoclopramide 5 mg/ml Injection should be protected from light during infusion. Degradation is indicated by a yellow discoloration. Such solution must not be used.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Protect from light and store in a cool place.

6.5 Nature and contents of container

Type I clear glass ampoules 2 ml, 10 ml and 20 ml packed in cardboard cartons to contain 10 ampoules in each.

6.6 Instructions for use, handling and disposal

Use as directed by a physician.

ADMINISTRATIVE DATA

7. MARKETING AUTHORISATION HOLDER

hameln pharmaceuticals ltd
Gloucester
UK

8. MARKETING AUTHORISATION NUMBER

PL 01502/0044

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

16th August 1996

10. DATE OF (PARTIAL) REVISION OF TEXT

30th December 2011