

## **1. NAME OF THE MEDICINAL PRODUCT**

Metoclopramide Injection BP 10mg/2ml

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each 2ml contains 5.27mg (0.527% w/v) Metoclopramide Hydrochloride BP equivalent to 10mg Anhydrous Metoclopramide Hydrochloride.

## **3. PHARMACEUTICAL FORM**

Solution for injection.  
Clear, colourless, sterile solution.

## **4 CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

1) For relief of symptoms of the upper digestive tract, including dyspepsia, flatulence, heartburn, nausea and pain associated with such conditions as: peptic ulcer, reflux oesophagitis, gastritis, duodenitis, cholelithiasis, hiatus hernia, dyspepsia following cholecystectomy.

2) As an anti-emetic for the treatment of nausea and vomiting associated with gastrointestinal disorders, intolerance to cytotoxic drugs, congestive heart failure, cyclical vomiting, migraine, radiotherapy/ cobalt therapy or post-anaesthetic vomiting. Metoclopramide relieves symptoms of nausea and vomiting, and overcomes gastric stasis associated with attacks of migraine. This improvement in gastric emptying assists the absorption of concurrently administered oral anti-migraine therapy (e.g. paracetamol) which may otherwise be impaired in such patients.

3) To promote normal gastric emptying and to restore motility in vagotomised patients and where post-operative symptoms suggest gastro-duodenal dysfunction.

4) For diagnostic procedures, to facilitate barium meal examinations and intubation procedures. Metoclopramide speeds up the passage of a barium meal by decreasing gastric emptying time, co-ordinating peristalsis and dilating the duodenal bulb. Metoclopramide also facilitates duodenal intubation procedures.

Young adults and children: The use of metoclopramide in patients under 20 years should be confined to the following: severe intractable vomiting of known cause; vomiting associated with radiotherapy and intolerance to cytotoxic drugs; facilitation of gastrointestinal intubation; as part of a premedication prior to surgical procedures.

#### **4.2. Posology and Method of Administration**

Route of administration: Intramuscular, or slow intravenous injection (1 - 2 minutes).

The dosage recommendations shown below should be followed strictly, if side-effects of the dystonic type are to be avoided. It should be noted that the total daily dosage of metoclopramide should not normally exceed 0.5mg/kg body weight, and this is especially important in the case of children and young adults. The dosage of metoclopramide should be reduced in patients with clinically significant degrees of renal or hepatic impairment. Metoclopramide is metabolised in the liver and is excreted via the kidney

##### Medical indications

*Adults age 20 years and over:*

10mg three times daily. For patients of less than 60kg body weight, see below.

*Elderly patients:*

As for adults. The dosage recommendations should be followed, carefully, if adverse reactions are to be avoided. Patients on prolonged therapy with metoclopramide should be reviewed regularly.

*Young adults and children:*

Before administering metoclopramide, careful examination is required in order to avoid masking any underlying disorders such as cerebral irritation. In order to minimise the risk of dystonic reactions, the following dosage recommendations should be strictly adhered to and treatment should commence at the lower dosage where stated.

*Young adults 15—19 years:*

60kg and over; 10mg three times daily.

30—59kg; 5mg three times daily.

*Children:*

9— 14 years: 30kg and over; 5mg three times daily.

5—9 years: 20—29kg; 2.5mg three times daily.

3—5 years: 15— 19kg; 2mg two to three times daily.

1 —3 years: 10 — 14kg; 1mg two to three times daily.

Under 1 year: Up to 10kg; 1mg twice daily.

##### Diagnostic Indications:

A single dose of metoclopramide may be given 5 — 10 minutes before the examination. Subject to body weight considerations (see above), the following dosages are recommended:

Adults (20 years and over); 10— 20mg

Young adults (15—19 years); 10mg

Children (9— 14 years); 5mg  
(5—9 years); 2.5mg  
(3—5 years); 2mg  
(Under 3 years); 1mg

### **4.3 Contraindications**

It is contra-indicated in patients who have previously shown hypersensitivity to metoclopramide or any of its components.

It should not be used in patients with phaeochromocytoma as it may induce an acute hypertensive response.

It 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.

It should not be administered to patients with gastrointestinal obstruction, perforation or haemorrhage.

### **4.4 Special warnings and precautions for use**

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

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

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

Extrapyramidal symptoms may occur with both metoclopramide and neuroleptics and care is required if these drugs are being used concurrently.

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.

Special care should be taken in cases of severe renal and hepatic insufficiency (see also section 4.2 Posology and method of administration).

#### **4.5. Interactions with other Medicinal Products and other Forms of Interaction**

**Anticholinergics and opioid analgesics:** These drugs antagonise the action of metoclopramide on the gastro-intestinal tract.

**Aspirin and paracetamol:** The effect of metoclopramide on gastric motility may modify the absorption of other concurrently administered oral drugs from the gastro-intestinal tract.

**Phenothiazines and Tetrabenazine:** Since extrapyramidal reactions may occur with Metoclopramide, care should be exercised in the event of co-administration of these drugs.

**Anti-Parkinson agents and other drugs acting at central dopamine receptors:**

The effects of anti-Parkinson agents such as levodopa, pergolide and ropinirole may be reduced. Metoclopramide may antagonise the hypoprolactinaemic effect of prolactin and medications such as cabergoline.

Metoclopramide should be used with care in association with other drugs acting at central dopamine receptors, such as bromocriptine.

**Serotonergic drugs:** The use of Metoclopramide with these drugs may increase the risk of serotonin syndrome.

**Atovaquone:** Metoclopramide may reduce its plasma concentrations.

**Ciclosporin:** Metoclopramide can increase the systemic availability of ciclosporin. Its level should be monitored.

**Suxamethonium:** Metoclopramide enhances its effects.

#### **4.6 Pregnancy and lactation**

Neither clinical experience nor animal tests in several mammalian species have indicated a teratogenic effect. However, metoclopramide should be used during pregnancy only if considered essential by the physician and the drug is not recommended during the first trimester. During lactation, metoclopramide is found in breast milk, therefore it should not be used during lactation.

#### **4.7. Effects on Ability to Drive and Use Machines**

Rarely, drowsiness may occur and patients should be warned not to drive or to operate machinery if affected.

#### 4.8 Undesirable effects

##### **Blood and lymphatic disorders:**

Very rare (<1/10,000): Cases of red cell disorders such as methaemoglobinaemia and sulphaemoglobinaemia have been reported, particularly at high doses of Metoclopramide. If this occurs the drug should be withdrawn. Methaemoglobinaemia may be treated using methylene blue.

##### **Cardiac disorders:**

Very rare (<1/10,000): Reports of abnormalities of cardiac conduction (such as bradycardia and heart block) in association with intravenous metoclopramide.

##### **Gastrointestinal disorders:**

Very rare (<1/10,000): Constipation, oedema of tongue

Rare ( $\geq$ 1/10,000 to <1/1,000): Diarrhoea

##### **Immune system disorders:**

Very rare (<1/10,000): hypersensitivity, including anaphylaxis has been reported.

**Investigations:** Increased serum levels of prolactin, resulting in irregular periods.

**Nervous system disorders:** Various extra-pyramidal reactions to metoclopramide have been reported. These are usually of the dystonic type and include facial spasm, trismus, rhythmic protrusions of the tongue, a bulbar type of speech, extra-ocular muscle spasm including oculogyric crises, unnatural positioning of the head and shoulders and opisthotonus. There may be a generalised increase in muscle tone. The incidence of these reactions, especially in children and young adults, is increased if daily dosages higher than 0.5mg per kg body weight are given. The majority of such reactions occur within 36 hours of commencing therapy and the effects usually disappear with 24 hours of withdrawal of the drug. If treatment of a dystonic reaction is required, an anticholinergic anti-Parkinsonian drug or a benzodiazepine may be given.

Very rare (<1/10,000): Occurrences of the 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.

Rarely ( $\geq$ 1/10,000 to <1/1,000) drowsiness, restlessness, dizziness, faintness, agitation, confusion.

Tardive dyskinesia has been reported in a small number of mainly elderly patients during prolonged treatment with metoclopramide. Patients on prolonged treatment should be reviewed, regularly.

**Psychiatric disorder:**

Very rare (<1/10,000): anxiety, depression.

**Reproductive system and breast disorders:**

Galactorrhea and gynaecomastia have been reported.

**Skin and subcutaneous tissue disorders:**

Very rare (<1/10,000): Skin rashes.

A small number of skin reactions such as urticaria, pruritus and oedema have also been reported.

**Vascular disorders:**

Very rare (<1/10,000): Hypotension

## 4.9 Overdose

Possible symptoms of overdosage include drowsiness, disorientation and extrapyramidal reactions. Acute dystonic reactions have occurred.

Very rarely AV block has been observed.

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. 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

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 gastro-intestinal motility is a common underlying factor.

Metoclopramide stimulates activity of the upper gastro-intestinal tract and restores normal co-ordination and tone. Gastric emptying is accelerated and the resting tone of the gastrooesophageal

sphincter is increased. Metoclopramide is a dopamine-receptor antagonist with a direct anti-emetic effect on the medullary chemoreceptor trigger zone.

## **5.2. Pharmacokinetic Properties**

Metoclopramide is rapidly absorbed from the gastrointestinal tract and undergoes variable first-pass metabolism in the liver. It is excreted mainly in the urine as free and as conjugated metoclopramide and as metabolites. It crosses the placenta and is excreted in breast milk. The elimination half-life is about 6 hours and may be prolonged in patients with renal failure or hepatic impairment.

## **5.3. Pre-clinical Safety Data**

No further relevant information other than that which is included with other sections of the Summary of Product Characteristics.

# **6. PHARMACEUTICAL PARTICULARS**

## **6.1. List of Excipients**

Sodium Metabisulphite, Sodium Chloride, Dilute Hydrochloric Acid or Sodium Hydroxide, Water for Injections.

## **6.2. Incompatibilities**

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

## **6.3. Shelf-Life**

3 years (36 months).

## **6.4 Special precautions for storage**

Do not store above 25°C.

Keep in the outer carton, protect from light.

## **6.5. Nature and Contents of Container**

2ml, clear glass ampoules, glass type 1 Ph.Eur. borosilicate glass packed in cardboard cartons to contain 10 x 2ml ampoules.

**6.6. Instruction for Use, Handling and Disposal**

If only part of an ampoule is used, discard the remaining solution.

**7. MARKETING AUTHORISATION HOLDER**

Antigen International Limited  
Roscrea,  
Co. Tipperary,  
Ireland.

**8. MARKETING AUTHORISATION NUMBER**

PL 2848/0113.

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION**

Date of first authorisation: 29/7/83.  
Date of renewal 24/2/89.

**10 DATE OF REVISION OF THE TEXT**

15/12/2010