## PROFESSIONAL INFORMATION

## SCHEDULING STATUS

S4

## 1 NAME OF THE MEDICINE

**Pharma-Q Metoclopramide Injection 10 mg/2 ml** solution for injection

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2 ml contains: 10 mg Metoclopramide base as hydrochloride monohydrate. For full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution in clear, colourless, type 1, glass ampoules.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Pharma-Q Metoclopramide Injection 10 mg/2 ml is used in the treatment of:

- Gastro-intestinal motility disorders.
- Nausea and vomiting of various causes.
- Medicine-induced post-operative nausea and vomiting.

**It is also used in disorders of:**

- Reduced gastro-intestinal motility such as gastroparesis or ileus.
- Gastro-oesophageal reflux and dyspepsia.
- Nausea and vomiting associated with various gastro-intestinal disorders.
- Gastric stasis or hypomotility.
- Migraine or following surgery.
- Cancer chemotherapy and radiotherapy.

Pharma-Q Metoclopramide Injection 10 mg/2 ml may also be used to:

- Stimulate gastric emptying during radio-graphic examinations of the stomach and/or small intestines.
- Facilitate intubation of the small bowel.

## 4.2 Posology and method of administration

**Posology**

Pharma-Q Metoclopramide Injection 10 mg/2 ml:

***Adults:***

- Potency is expressed in terms of anhydrous metoclopramide and doses of 10 to 15 mg can be administered by intramuscular or slow intravenous injection, up to four times daily.
- Single doses should be considered where appropriate and single doses of up to 20 mg, expressed as anhydrous base have been used.

***Young adults and children:***

Doses should be reduced in young adults and in children because of the risk of dystonic reactions.

- 15 to 19 years of age:
    - 5 mg three times daily for those weighing 30 to 59 kg.
    - 10 mg three times daily for those weighing 60 kg and over.
- 9 to 14 years of age:
    - 5 mg three times daily for those weighing 30 kg and over.
- 5 to 9 years of age:
    - 2,5 mg three times daily for those weighing 20 to 29 kg.
- 3 to 5 years of age:
    - 1 mg two to three times daily for those weighing 15 to 19 kg.
- 1 to 3 years of age:
    - 0,5 mg two to three times daily for those weighing 10 to 14 kg.

Where body-weight is below that specified for a given dosage group, the dose should reflect the weight rather than the age, so that a lower dose is chosen.

## 4.3 Contraindications

- Hypersensitivity to metoclopramide 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)

## 4.4 Special warnings and precautions for use

***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. Pharma-Q Metoclopramide Injection 10 mg/2 ml 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 medicines in adults).

Since extrapyramidal symptoms may occur with both metoclopramide and neuroleptics such as the phenothiazines, particular care should be exercised in the event of these medicines being

prescribed concurrently.

The time interval of at least 6 hours specified in the section 4.2 should be respected between each Pharma-Q Metoclopramide Injection 10 mg/2 ml administration, even in case of vomiting and rejection of the dose, in order to avoid overdose.

Prolonged treatment with Pharma-Q Metoclopramide Injection 10 mg/2 ml 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). Pharma-Q Metoclopramide Injection 10 mg/2 ml 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 medicines (see section 4.3)

Symptoms of Parkinson's disease may also be exacerbated by Pharma-Q Metoclopramide Injection 10 mg/2 ml.

***Methaemoglobinemia***

Methemoglobinemia which could be related to NADH cytochrome b5 reductase deficiency has been reported. In such cases, Pharma-Q Metoclopramide Injection 10 mg/2 ml 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 Pharma-Q Metoclopramide Injection 10 mg/2 ml, 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 medicines 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).

Risk-benefit should be carefully considered in patients with significant hepatic or renal impairment (loss of conjugation and increased risk of extrapyramidal effects) or with Parkinson's disease (symptoms may be exacerbated).

**Precautions**

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 patients being treated with other centrally acting medicines.

Pharma-Q Metoclopramide Injection 10 mg/2 ml should be used with care in combination with other serotonergic medicines including SSRIs.

Patients receiving Pharma-Q Metoclopramide Injection 10 mg/2 ml for the disorders associated with delayed gastric emptying should be reviewed at an early stage for response to treatment.

Pharma-Q Metoclopramide Injection 10 mg/2 ml may cause elevation of serum prolactin levels.

Care should be exercised when using Pharma-Q Metoclopramide Injection 10 mg/2 ml in patients with a history of atopy (including asthma) or porphyria.

## 4.5 Interaction with other medicines and other forms of interaction

***Contraindicated combination***

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

Pharma-Q Metoclopramide Injection 10 mg/2 ml should be used with care in association with other medicines acting at central dopamine receptors such as bromocriptine and pergolide.

***Combination to be avoided***

Alcohol potentiates the sedative effect of Pharma-Q Metoclopramide Injection 10 mg/2 ml.

***Combination to be taken into account***

Due to the prokinetic effect of metoclopramide, the absorption of certain medicines may be modified.

*Anticholinergics, morphine derivatives and other opioid analgesics*

Anticholinergics and morphine derivatives may have both a mutual antagonism with Pharma-Q Metoclopramide Injection 10 mg/2 ml on the digestive tract motility.

The absorption of aspirin and paracetamol may be modified by the effect of Pharma-Q Metoclopramide Injection 10 mg/2 ml on gastric motility.

Concomitant use of anticholinergic medicines may inhibit the favourable effects on gastrointestinal motility.

Since extrapyramidal reactions may occur with Pharma-Q Metoclopramide Injection 10 mg/2 ml, phenothiazines and tetrabenazine, care should be exercised in the event of co-administration of these medicines.

*Central nervous system depressants (morphine derivatives, anxiolytics, sedative H1 antihistamines, sedative antidepressants, barbiturates, clonidine and related)*

Sedative effects of central nervous system depressants and Pharma-Q Metoclopramide

Injection 10 mg/2 ml are potentiated.

*Neuroleptics*

Pharma-Q Metoclopramide Injection 10 mg/2 ml may have an additive effect with other neuroleptics on the occurrence of extrapyramidal disorders.

*Monoamine oxidase inhibitors*

The effects of certain other medicines with potential central stimulant effects, e.g. monoamine oxidase inhibitors and sympathomimetics, may be modified when prescribed with Pharma-Q Metoclopramide Injection 10 mg/2 ml and their dosage may need to be adjusted accordingly.

*Serotonergic medicines*

The use of Pharma-Q Metoclopramide Injection 10 mg/2 ml with serotonergic medicines such as SSRIs may increase the risk of serotonin syndrome.

*Digoxin*

Pharma-Q Metoclopramide Injection 10 mg/2 ml may decrease digoxin bioavailability. Careful monitoring of digoxin plasma concentration is required.

*Ciclosporine*

Metoclopramide increases ciclosporine bioavailability ($C_{max}$ by 46 % and exposure by 22 %). Careful monitoring of ciclosporine plasma concentration is required. The clinical consequence is uncertain.

*Mivacurium and suxamethonium*

Pharma-Q Metoclopramide Injection 10 mg/2 ml 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.

*Antiprotozoals*

Pharma-Q Metoclopramide Injection 10 mg/2 ml may reduce plasma concentrations of atovaquone.

## 4.6 Fertility, pregnancy and lactation

The safety of Pharma-Q Metoclopramide Injection 10 mg/2 ml in pregnant and lactating women has not been established (see section 4.3).

***Pregnancy***

A large amount of data on pregnant women (more than 1 000 exposed outcomes) indicates no malformative toxicity nor foetotoxicity. Due to pharmacological properties (as other neuroleptics), in case of Pharma-Q Metoclopramide Injection 10 mg/2 ml administration at the end of pregnancy, extrapyramidal syndrome in newborn cannot be excluded. Pharma-Q Metoclopramide Injection 10 mg/2 ml should be avoided at the end of pregnancy. If Pharma-Q Metoclopramide Injection 10 mg/2 ml 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 Pharma-Q Metoclopramide Injection 10 mg/2 ml is not recommended during breastfeeding. Discontinuation of Pharma-Q Metoclopramide Injection 10 mg/2 ml in breastfeeding women should be considered.

## 4.7 Effects on ability to drive and use machines

Pharma-Q Metoclopramide Injection 10 mg/2 ml may cause drowsiness, dizziness, dyskinesia

and dystonias which could affect the vision. Patients affected should not drive or operate machinery.

### 4.8 Undesirable effects

**Tabulated summary of adverse reactions**

Adverse reactions listed by System Organ Class. Frequencies are defined using the following convention: frequent, less frequent or frequency unknown (cannot be estimated from the available data).

| **MedDRA system organ class** | **Frequency** | **Adverse reactions** |
|---|---|---|
| Blood and the lymphatic system disorders | Frequency unknown | 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 medicines |
| Immune system disorders | Less frequent | Hypersensitivity |
| | Frequency unknown | Anaphylactic reaction (including anaphylactic shock particularly with intravenous formulation) |
| Endocrine disorders | Less frequent | Amenorrhoea, hyperprolactinaemia, galactorrhoea |
| | Frequency unknown | Gynaecomastia |
| Psychiatric disorders | Frequent | Depression |
| | Less frequent | Hallucination, confusional state |

| **MedDRA system organ class** | **Frequency** | **Adverse reactions** |
|---|---|---|
| Nervous system disorders | Frequent | Somnolence, 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 medicine) (see section 4.4), parkinsonism, akathisia |
| | Less frequent | Dystonia including oculogyric crisis, dyskinesia, depressed level of consciousness, convulsion especially in epileptic patients |
| | Frequency unknown | 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 | Less frequent | Bradycardia, particularly with intravenous formulation |
| | Frequency unknown | 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; dyspnoea |
| Vascular disorders | Frequent | Hypotension, particularly with intravenous formulation |

| MedDRA system organ class | Frequency | Adverse reactions |
|---|---|---|
| | Frequency unknown | Shock, syncope after injectable use, acute hypertension in patients with pheochromocytoma (see section 4.3), transient increase in blood pressure |
| Gastrointestinal disorders | Frequent | Diarrhoea |
| General disorders and administration site conditions | Frequent | 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 medicine, 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 medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Medicine Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

### 4.9 Overdose

**Signs and symptoms**

In cases of overdosage, acute dystonic/extrapyramidal reactions have occurred. Very rarely AV block has been observed.

Drowsiness, decreased level of consciousness, confusion, hallucination, and cardio-respiratory arrest may occur.

**Management of overdose**

In case of extrapyramidal symptoms related or not to overdose, the treatment is only symptomatic (benzodiazepines in children and/or anticholinergic anti-parkinsonian medicines 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: Agents stimulating gastro-intestinal motility

ATC Code: A03FA01

Metoclopramide hydrochloride enhances the motility of smooth muscle of the upper gastrointestinal tract.

### 5.2 Pharmacokinetic properties

It is distributed rapidly into most tissues and readily crosses the blood-brain barrier and the placenta. Up to 30 % of metoclopramide is excreted unchanged in the urine and the remainder is eliminated in the urine and the bile after conjugation with sulfate or glucuronic acid. The half-life is about 4 to 6 hours, but may be as much as 24 hours in patients with impaired renal function.

### 5.3 Preclinical safety data

No additional data available.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Hydrochloric acid

Nitrogen

Sodium chloride

Water for injection

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

24 months

### 6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light.

Reject ampoules showing a yellow discolouration.

### 6.5 Nature and contents of container

2 ml, type 1, clear, colourless, glass ampoules packed in cartons of 10 or 100.

### 6.6 Special precautions for disposal

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

## 7 HOLDER OF CERTIFICATE OF REGISTRATION

Pharma-Q Holdings (Pty) Ltd

50 Commando Road

Industria West 2003

Johannesburg

South Africa

## 8 REGISTRATION NUMBER

34/5.7.2/0051

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 February 2006

## 10 DATE OF REVISION OF THE TEXT

29 August 2011

## PROFESSIONELE INLIGTING

### SKEDULERINGSTATUS

S4

## 1 NAAM VAN DIE MEDISYNE

**Pharma-Q Metoclopramide Injection 10 mg/2 ml** oplossing vir inspuiting

## 2 KWALITATIEWE EN KWANTITATIEWE SAMESTELLING

Elke 2 ml bevat: 10 mg Metoklopramied basis as hidrochloriedmonohidraat. Vir die volle lys van ander bestanddele, sien afdeling 6.1

## 3 FARMASEUTIESE VORM

Oplossing vir inspuiting.

Helder, kleurlose oplossing in deursigtige, kleurlose, tipe 1, glas ampules.

## 4 KLINIESE BESONDERHEDE

### 4.1 Terapeutiese indikasies

Pharma-Q Metoclopramide Injection 10 mg/2 ml word gebruik vir die behandeling van:

- Gastroïntestinale beweeglikheidsversteurings.
- Naarheid en braking van verskeie oorsake.
- Medisyne geïnduseerde post-operatiewe naarheid en braking.

**Dit word ook gebruik vir die versteurings van:**

- Verminderde gastroïntestinale beweeglikheid soos gastroparese of ileus.
- Gastroësofaqeale refluks en dispepsie.
- Naarheid en braking geassosieer met verskeie gastroïntestinale versteurings.
- Maagstase of hipomotiliteit
- Migraine of na 'n operasie.
- Kanker chemoterapie en bestraling.

Pharma-Q Metoclopramide Injection 10 mg/2 ml kan ook gebruik word vir:

- Stimuleer maaglediging tydens radiografiese ondersoeke van die maag en/of dunderm.
- Fasiliteer intubasie van die dunderm

## 4.2 Posologie en metode van toediening

**Posologie**

Pharma-Q Metoclopramide Injection 10 mg/2 ml:

***Volwassenes:***

- Sterkte word uitgedruk in terme van anhidriese metoklopramied en doserings van 10 tot 15 mg kan toegedien word deur intramuskulêre of stadige intraveneuse inspuiting, tot vierkeer per dag.
- Enkel doserings moet oorweeg word waar toepaslik en enkeldoserings van tot 20 mg, uitgedruk as anhidriese basis is gebruik.

***Jong volwassenes en kinders:***

Dosisse moet verlaag word in jong volwassesnes en by kinders as gevolg van die risiko van distoniese reaksies

- 15 tot 19 jaar oud:
    - 5 mg driekeer per dag vir diegene wat 30 tot 59 kg weeg
    - 10 mg driekeer per dag vir diegene wat 60 kg en meer weeg
- 9 tot 14 jaar oud:
    - 5 mg driekeer per dag vir diegene wat 30 kg en meer weeg
- 5 tot 9 jaar oud:
    - 2,5 mg driekeer per dag vir diegene wat 20 tot 29 kg weeg
- 3 tot 5 jaar oud:
    - 1 mg twee to driekeer per dag vir diegene wat 15 tot 19 kg weeg
- 1 tot 3 jaar oud:
    - 0,5 mg twee tot driekeer per dag vir diegene wat 10 tot 14 kg weeg

Waar liggaamsgewig, laer is as wat gespesifiseer word vir 'n gegewe doseringsgroep, moet die dosis die gewig eerder as die ouderdom reflekteer, sodat 'n laer dosis gekies word.

## 4.3 Kontraindikasies

- Hipersensitiwiteit vir metoklopramied of vir enige van die ander bestanddele in afdeling 6.1.
- Gastroïntestinale bloeding, meganiese obstruksie of gastroïntestinale perforasie waarvoor die stimulering van spysverteringskanaal beweeglikheid 'n risiko inhou
- Bevestigde of vermoedelike feochromositoom, as gevolg van die risiko van erge hipertensiewe episodes.
- Geskiedenis van neuroleptiese of metoklopramied geïnduseerde tardiewe diskinesie.
- Epilepsie (verhoogde krisis frekwensie en intensiteit)
- Parkinson se siekte
- Kombinasie met levodopa of dopamienerge agoniste (sien afdeling 4.5).
- Bekende geskiedenis van methemoglobinemie met metoklopramied of van NADH sitochroom-b5 tekort.
- Gebruik by kinders jonger as 1 jaar oud as gevolg van verhoogde risiko van ekstrapiramidale versteurings (sien afedling 4.4)

## 4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik

***Neurologiese versteurings***

Ekstrapiramidale versteurings kan voorkom, veral by kinders en jong volwassenes, en/of wanneer hoë dossise gebruik word. Hierdie reaksies kom gewoonlik aan die begin van die behandeling voor en kan na 'n enkele toediening voorkom. Pharma-Q Metoclopramide Injection 10 mg/2 ml moet onmidelik gestaak word in geval van ekstrapiramidale simptome. Hierdie effekte is gewoonlik total omkeerbaar na staking van behandeling, maar kan 'n simptomaties behandeling benodig (bensodiasepiene in kinders en/of anticholinergiese anti-Parkinsonistiese medisyne by volwassenes).

Aangesien ekstrapiramidale simptome mag voorkom met beide metoklopramied en neuroleptika soos die fenotiasiene, moet daar spesiale sorg getref word indien hierdie medisyne terselfdertyd voorgeskryf word.

Die tydsinterval van ten minste 6 ure gespesifiseer in hierdie afdeling 4.2 moet grespekteer word tussen elke Pharma-Q Metoclopramide Injection 10 mg/2 ml toediening, selfs in geval van braking en verwerping van die dosis, om sodoende oordosering te voorkom.

Langdurige behandeling met Pharma-Q Metoclopramide Injection 10 mg/2 ml kan tardiewe diskinesie, moontlike onomkeerbaar, veral by bejaardes. Behandeling moet nie 3 maande oorskrei nie as gevolg van die risiko van tardiewe diskinesie (sien afdeling 4.8). Behandeling moet gestaak word indien kliniese tekens van tardiewe diskinesie voorkom.

Neuroleptiese kwaadaardige sindroom is aangemeld met metoklopramied in kombinasie met neuroleptika sowel as met metoklopramied monoterapie (sien afdeling 4.8). Pharma-Q Metoclopramide Injection 10 mg/2 ml moet onmiddelik gestaak word in geval van neuroleptiese kwaadaardige sindroom en toepaslike behandeling moet begin word.

Spesiale sorg moet aan die dag gelê word by pasiënte met onderliggende neurologiese toestande en by pasiënte behandel met ander sentraalwerkende medisyne (sien afdeling 4.3)

Simptome van Parkinson se siekte kan ook vererger word deur Pharma-Q Metoclopramide Injection 10 mg/2 ml.

***Methemoglobinemie***

Methemoglobinemie wat verwant kan wees aan NADH sitochroom b5 reduktase tekort is aangemeld. In sulke gevalle moet Pharma-Q Metoclopramide Injection 10 mg/2 ml onmiddelik en permanent gestaak word en toepaslike maatreëls ingestel word (soos behandeling met metileen blou).

***Kardiale versteurings***

Ernstige kardiovaskulêre ongewenste effekte is aangemeld, insluitende gevalle van sirkulatoriese ineenstorting, erge bradikardie, kardiale arres en QT verlenging na toediening van

metoklopramied deur inspuiting, veral via die intraveneuse roete (sien afdeling 4.8)

Spesiale sorg moet aan die dag gelê word wanneer Pharma-Q Metoclopramide Injection 10 mg/2 ml toegedien word aan die bejaarde populasie, veral via die intraveneuse roete, by pasiënte met hartgeleidings versteurings (insluitende QT verlenging), pasiënte met ongekorrigeerde elektroliet wanbalans, bradikardie en die wat ander medisyne neem wat bekend is vir QT interval verlenging.

Intraveneuse doserings moet as 'n stadige bolus toegedien word (ten minste oor 3 minute) om sodoende die risiko van newe-effekte (bv hipotensie, akatisie) te verminder.

***Renale en hepatiese ontoereikendheid***

By pasiënte met renale ontoereikendheid of erge hepatiese ontoereikendheid, word 'n dosisverlaging aanbeveel (sien afdeling 4.2).

Risiko-voordeel moet versigtig oorweeg word by pasiënte met beduidende hepatiese of renale ontoereikendheid (verlies van konjugering en 'n verhoogde risiko vir ekstrapiramidale effekte) of met Parkinson se siekte (simptome mag vererger word).

**Voorsorgmaatreëls**

Indien braking voortduur, moet die pasiënt heroorweeg word om die moontlikheid van 'n onderliggende versteuring uit te sluit, bv. serebrale irritasie.

Sorg moet gedra word by pasiënte wat met ander sentraalwerkende medisyne behandel word.

Pharma-Q Metoclopramide Injection 10 mg/2 ml moet versigtig gebruik word in kombinasie met ander serotonergiese medisyne, insluitend SSRI's.

Pasiënte wat Pharma-Q Metoclopramide Injection 10 mg/2 ml ontvang vir die afwykings wat verband hou met vertraagde maaglediging, moet in 'n vroeë stadium hersien word vir reaksie op die behandeling.

Pharma-Q Metoclopramide Injection 10 mg/2 ml kan verhoogde serumprolaktienvlakke veroorsaak.

Sorg moet gedra word wanneer u Pharma-Q Metoclopramide Injection 10 mg/2 ml gebruik by

pasiënte met 'n geskiedenis van atopie (insluitend asma) of porfirie.

## 4.5 Interaksies met ander medisyne en ander vorms van interaksie

***Gekontraïndikeerde kombinasie***

Levodopa of dopaminerge agoniste en metokloparnied het 'n gemene antgonisme (sien afdeling 4.3)

Pharma-Q Metoclopramide Injection 10 mg/2 ml moet met versigtigheid gebruik word tesame met ander medikasie wat op die sentrale dopamien reseptore werk soos bromokriptien en pergolied.

***Kombinasie wat vermy moet word***

Alkohol potensieer die sedatiewe effek van metoklopramied van Pharma-Q Metoclopramide Injection 10 mg/2 ml.

***Kombinasie wat in ag geneem moet word***

As gevolg van die prokinetiese effek van metoklopramied, kan die absorpise van sekere medisyne verander word.

*Anticholinergiese middels, morfien derivate en ander opioïed analgetika*

Anticholinergiese middels en morfien derivate kan albei 'n wedersydse antagonisme met Pharma-Q Metoclopramide Injection 10 mg/2 ml op die spysverteringskanaal beweeglikheid hê Die absorpsie van aspirien en parasetamol kan verander word deur die effek van Pharma-Q Metoclopramide Injection 10 mg/2 ml op gastriese beweeglikheid.

Tegelyktydige gebruik van anticholinergiese mediysne kan die voordelige effekte op gastroïntestinale beweeglikheid verander.

Aangesien ekstrapiramidale reaksies met Pharma-Q Metoclopramide Injection 10 mg/2 ml, fenotiasiene en tertrabenisien, kan voorkom, moet sorg gedra word in die geval van gelyktydige toediening van hierdie medisyne.

*Sentrale senuweestelsel onderdrukkers (morfien derivate, anksiolitiese middels, sedatiewe H1 antihistamiene, sedatiewe antidepressante, barbiturate, klonidien en verwante)*

Sedatiewe effekte van sentrale senuweestelsel onderdrukkers en Pharma-Q Metoclopramide Injection 10 mg/2 ml word gepotensieer.

*Neuroleptika*

Pharma-Q Metoclopramide Injection 10 mg/2 ml kan 'n bydraende effek hê op die voorkoms van ekstrapiramidale effekte saam met ander neuroleptika

*Monoamien oksidase inhibeerders*

Die effek van sekere ander medisyne met potensiële sentrale stimulant effekte, bv. monoamien oksidase inhibeerders en simpatomimetika, kan verander word wanneer voorgeskryf word saam met Pharma-Q Metoclopramide Injection 10 mg/2 ml en dit mag nodig wees om die dosering dienooreenkomstig aan te pas.

*Serotonergiese medisyne*

Die gebruik van Pharma-Q Metoclopramide Injection 10 mg/2 ml saam met serotonergiese medisyne soos SSRI's kan die risiko van serotonien sindroom verhoog.

*Digoksien*

Pharma-Q Metoclopramide Injection 10 mg/2 ml kan digoksien biobeskikbaarheid verlaag. Versigtige monitering van digoksien plasma konsentrasies word vereis.

*Siklosporiene*

Metoklopramied verhoog siklosporien biobeskikbaarheid ($C_{max}$ 46 % en blootstelling 22 %) Versigtige monitering van siklosporien plasmakonsentrasies word vereis. Die kliniese nagevolge is onseker.

*Mivakurium en suksametonium*

Pharma-Q Metoclopramide Injection 10 mg/2 ml kan die duur van neuromuskulêre blok verleng (deur inhibering van plasma cholienesterase)

*Sterk CYP2D6 inhibeerders*

Metoklopramied blootstellingsvlakke word verhoog wanneer tesame met sterk CYP2D6 inhibeerders soos fluoksetien en paroksetien toegedien word. Alhoewel die kliniese betekenis onseker is, moet pasiënte met newe-effekte gemonitor word.

*Antiprotosoale middels*

Pharma-Q Metoclopramide Injection 10 mg/2 ml kan plasmakonsentrasies van atovakoon verlaag.

**4.6 Fertiliteit, swangerskap en laktasie**

Die veiligheid van Pharma-Q Metoclopramide Injection 10 mg/2 ml in swanger en borsvoedende vroue is nog nie vasgestel nie (sien afdeling 4.3).

***Swangerskap***

'n Groot aantal data by swanger vroue (meer as 1 000 blootgestelde uitkomste) wys geen wanvormende toksisiteit of fetotoksisiteit nie. As gevolg van farmakologiese eienskappe (soos ander neuroleptika), in geval van Pharma-Q Metoclopramide Injection 10 mg/2 ml toediening aan die einde van swangerskap, kan ekstrapiramidale simptome by die pasgeborene nie uitgesluit word nie. Pharma-Q Metoclopramide Injection 10 mg/2 ml moet vermy word aan die einde van swangerskap. Indien Pharma-Q Metoclopramide Injection 10 mg/2 ml gebruik word, moet neonatale monitering onderneem word.

***Borsvoeding***

Metoklopramied word in borsmelk uigeskei by 'n lae vlak. Newe-effekte by die borsgevoede baba kan nie uitgesluit word nie.

Daarom word Pharma-Q Metoclopramide Injection 10 mg/2 ml nie aanbeveel gedurende

borsvoeding nie. Staking van Pharma-Q Metoclopramide Injection 10 mg/2 ml moet oorweeg word by borsvoedende vrouens

### 4.7 Effek op die vermoë om te bestuur en gebruik van masjiene

Pharma-Q Metoclopramide Injection 10 mg/2 ml kan lomerigheid, duiseligheid, diskinesie en distonie veroorsaak, wat die visie kan affekteer.

Pasiënte wat geaffekteer word moet nie bestuur of masjiene gebruik nie.

### 4.8 Ongewenste effekte

**Opsomming van nadelige reaksies in tabelvorm**

Nadelige reaksies gelys volgens Sisteem Orgaan Klas. Frekwensies word gedefinieer volgens die volgende konvensie: gereeld, minder gereeld of frekwensie onbekend (kan nie geskat word van die beskikbare data)

| **MedDRA sisteem orgaan klas** | **Frekwensie** | **Newe-effek** |
|---|---|---|
| Bloed- en limfstelselversteurings | Frekwensie onbekend | Methemoglobinemie wat verwant kan wees aan NADH sitochroom b5 reduktase tekort, veral in neonate (sien afdeling 4.4 Sulfahemoglobinemie, hoofsaaklik met tegelyktydige toediening van hoë dosisse van sulfaatvrystellende medisyne. |
| Versteurings van die immuunstelsel | Minder gereeld | Hipersensitiwiteit |
| | Frekwensie onbekend | Anafilaktiese reaksie (insluitende anafilaktiese skok veral met intraveneuse formule) |
| Endokriene versteurings | Minder gereeld | Amenoree, hiperprolaktinemie, galaktoree |

| **MedDRA sisteem orgaan klas** | **Frekwensie** | **Newe-effek** |
|---|---|---|
| | Frekwensie onbekend | Ginekomastie |
| Psigiatriese versteurings | Gereeld | Depressie |
| | Minder gereeld | Hallusinasie, verwarringstaat |
| Senuweestelsel versteurings | Gereeld | Slaaploosheid, ekstrapiramidale versteurings (veral in kinders en jong volwassenes en/of wanneer die aanbevole dosis oorskrei word, selfs na toedieng van 'n enkeldosis van die medisyne) (sien afdeling 4.4), parkinsonisme. akatisie |
| | Minder gereeld | Distonie insluitende okulogiriese krisis, diskinesie, onderdrukte bewussynsvlak, konvulsie veral by epileptiese pasiënte |
| | Frekwensie onbekend | Tardiewe diskinesie wat aanhoudend kan wees tydens of na langdurige behandeling by bejaarde pasiënte (sien afdeling 4.4), neuroleptiese kwaadaardige sindroom (sien afdeling 4.4) |
| Kardiale versteurings | Minder gereeld | Bradikardie, veral met intraveneuse formule |
| | Frekwensie onbekend | Kardiale arres, wat voorkom kort na gebruik van inspuiting en wat kan volg op bradikardie (sien afdeling 4.4); atrioventrikulêre blok, sinus arres veral met intraveneuse formule; langdurige elektrokardiogram QT; Torsade de Pointes; dispnee |

| **MedDRA sisteem orgaan klas** | **Frekwensie** | **Newe-effek** |
|---|---|---|
| Vaskulêre versteurings | Gereeld | Hipotensie, veral met intraveneuse formule |
| | Frekwensie onbekend | Skok, sinkopee na inspuiting gebruik, akute hipertensie by pasiënte met feochromositoom (sien afdeling 4.3), verbygaande verhoging in bloeddruk |
| Gastroïntestinale versteurings | Gereeld | Diaree |
| Algemene versteurings en toedieningsplek-toestande | Gereeld | Astenie |

* Endokriene versteurings gedurende langdurige behandeling in verhouding met hiperprolaktinemie (amenoree, galaktoree, ginekomastie)

Die volgende reaksies, somtyds geassosieer, kom meer gereeld voor wanneer hoë dosisse gebruik word:

- Ekstrapiramidale simptome: akute distonie en diskinesie, parkinsonistiese sindroom, akatisie, selfs na toediening van 'n enkeldosis van die medisyne, veral by kinders en jong volwassenes (sien afdeling 4.4)
- Lomerigheid, verlaagde bewussynsvlakke, verwarring, hallusinasie

*Aanmelding van vermoedelike newe-effekte*

Aanmelding van vermoedelike newe-effekte na goedkeurig van die medisyne is belangrik. Dit laat voortdurende monitering van die voordeel/risiko balans van die medisyne toe, Gesondheidsorg werkers word gevra om enige vermoedelike newe-effekte aan SAHPRA aan te meld via die **"6.04 Adverse Medicine Reactions Reporting Form"**, wat aanlyn gevind kan word onder SAHPRA se publikasies:

https://www.sahpra.org.za/Publications/Index/8

### 4.9 Oordosering

**Tekens en simptome**

In geval van oordosering, het akute distonie/ekstrapiramidale reaksies voorgekom. AV blok is baie selde waargeneem.

Lomerigheid, verlaagde bewussynsvlakke, verwarring, hallusinasie en kardio-respiratories arres kan voorkom.

**Hantering van oordosering**

In geval van ekstrapiramidale simptome verwant aan oordosreing of nie, die behandeling is slegs simptomaties (bensodiasepiene in kinders en/of anticholinergiese anti-parkinsonistiese medisyne by volwassenes). 'n Simptomatiese behandeling en 'n volgehoue monitering van die kardiovaskulêre en respiratoriese funksies moet uitgevoer word volgens die kliniese status.

## 5 FARMAKOLOGIESE WERKING

### 5.1 Farmakodinamiese eienskappe

Farmakoterapeutiese groep: Middels wat gastroïntestinale motiliteit stimuleer

ATC Kode: A03FA01

Metoklopramied hidrochloried bevorder motiliteit van gladdespiere van die boonste spysverteringskanaal

### 5.2 Farmakokinetiese eienskappe

Dit word vinnig versprei in die meeste weefsel en kruis die bloedbreinskans en die plasenta geredelik. Tot 30 % metoklopramied word onveranderd in die uriene uitgeskei en die oorblywende word in die uriene en gal uitgeskei na konjugasie met sulfaat en glukuroniese suur. Die halfleeftyd is ongeveer 4 tot 6 ure, maar kan soveel as 24 uur wees by pasiënte met ingekorte nierfunksie.

### 5.3 Prekliniese veiligheidsdata

Geen addisionele data beskikbaar

## 6 FARMASEUTIESE BESONDERHEDE

### 6.1 Lys van ander bestanddele

Asynsuur

Stikstof

Natriumchloried

Water vir inspuiting

### 6.2 Onverenigbaarhede

Nie van toepassing

### 6.3 Rakleeftyd

24 maande

### 6.4 Spesiale voorsorgmaatreëls vir bewaring

Bewaar by of benede 25 °C.

Beskerm teen lig.

Verwerp ampules wat 'n geel kleur verkleuring wys.

### 6.5 Aard en inhoud van die houer

2 ml, tipe 1, deursigtige, kleurlose, glas ampules verpak in kartonne van 10 of 100.

### 6.6 Spesiale voorsorgmaatreëls vir vernietiging

Enige ongebruikte medisyne of afvalmateriaal, moet van ontslae geraak word in ooreenstemming met plaaslike vereistes.

## 7 HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE

Pharma-Q Holdings (Pty) Ltd

Commandoweg 50

Industria Wes 2003

Johannesburg

Suid-Afrika

## 8 REGISTRASIENOMMER

34/5.7.2/0051

## 9 DATUM VAN EERSTE GOEDKEURING/HERNUWING VAN DIE GOEDKEURING

17 Februarie 2006

## 10 DATUM VAN HERSIENING VAN DIE TEKS

29 Augustus 2011