PRODUCT MONOGRAPH

[Pr]pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION

Metoclopramide Hydrochloride Injection

Solution for Injection

5 mg / mL of Metoclopramide Hydrochloride

House Standard

Modifier of Upper Gastrointestinal Tract Motility– Antiemetic

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[Pr]pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION

Metoclopramide Hydrochloride Injection, House Standard
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5 mg / mL of Metoclopramide Hydrochloride

THERAPEUTIC CLASSIFICATION

Modifier of Upper Gastrointestinal Tract Motility – Antiemetic

ACTION AND CLINICAL PHARMACOLOGY

Metoclopramide is a benzamide derivative structurally related to procainamide and sulpiride. It has a dopamine antagonist activity with selective affinity for D2 (nonadenylate cyclase linked) receptors. The behavioural, motor and neuroendocrine effects of metoclopramide have been suggested to be due to its antidopaminergic activity.

Metoclopramide has antiemetic properties which are believed to result from its action on the chemoreceptor trigger zone. A peripheral mechanism of action may also be involved.

Metoclopramide raises resting pressure in the lower esophageal sphincter and the gastric fundus, and gives rise to an increase in the amplitude of peristaltic movements in the esophagus, gastric antrum and small intestine. As a consequence, esophageal clearance is hastened, gastric emptying accelerated and transit time through the small bowel shortened. These effects are blocked by atropine and opioids but not by vagotomy.

Metoclopramide elevates serum prolactin and causes transient increases in circulating aldosterone levels. These effects are thought to be due to blockade of dopamine receptors at the pituitary and adrenocortical cellular level.

Following intravenous administration, peak plasma levels occur within minutes. The terminal half-life is approximately 3 hours, but this is prolonged in patients with impaired renal function and may reach 14 hours or more. About 20% of the drug is eliminated unchanged in the urine, and 30 - 40% is eliminated as the sulfate conjugate. Metoclopramide is 15 - 20% bound to the plasma proteins.

In some patients, metoclopramide may produce drowsiness, sedation, galactorrhea, menstrual disorders and extrapyramidal reactions. Extrapyramidal symptoms are more frequent at higher than recommended doses, but may occur with therapeutic doses, particularly in children and in patients with impaired renal or hepatic function. Tardive dyskinesia has been reported following discontinuation of long-term treatment with metoclopramide.

INDICATIONS AND CLINICAL USE

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is useful as an adjunct in the management of delayed gastric emptying associated with subacute and chronic gastritis and sequelæ of surgical operations such as vagotomy and pyloroplasty.

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is indicated in the prophylaxis of vomiting induced by cancer chemotherapeutic regimens that include cisplatin as a component.

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION has been found useful as an adjunct to facilitate small bowel intubation.

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is indicated for the prophylaxis of postoperative vomiting.

CONTRAINDICATIONS

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is contraindicated whenever stimulation of the gastrointestinal motility may be dangerous, i.e. in the presence of gastrointestinal hemorrhage, perforation or mechanical obstruction. pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should not be used in patients with known sensitivity or intolerance to the drug. pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should not be used in epileptics or patients receiving other drugs which are likely to cause extrapyramidal reactions, since the frequency and severity of seizures or extrapyramidal reactions may be increased.

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is contraindicated in children less than one year of age

WARNINGS

Tardive dyskinesia has been reported to occur during long-term treatment (over 12 weeks) and following discontinuation of long-term treatment with metoclopramide.

The risk of developing tardive dyskinesia increases with the duration of treatment and the total cumulative dose. The elderly, especially elderly women are at increased risk of developing this condition.

Tardive Dyskinesia

Tardive dyskinesia may develop in patients treated with metoclopramide. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is not possible to predict which patients are likely to develop the syndrome.

Both risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase with the duration of treatment and the total cumulative dose.

Less commonly, the syndrome can develop after relatively brief treatment periods at low doses; in these cases, symptoms appear more likely to be reversible. Prolonged treatment (greater than 12 weeks) with pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should be avoided unless therapeutic benefit is thought to outweigh the risks to the patient developing tardive dyskinesia.

There is no known treatment for established cases of tardive dyskinesia although the syndrome may remit, partially or completely, within several weeks to months after pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION has been withdrawn.

Metoclopramide itself, however, may suppress (or partially suppress) the signs of tardive dyskinesia, thereby masking the underlying disease process. The effect of this symptomatic suppression upon the long-term course of the syndrome is unknown.

Other Extrapyramidal Symptoms (EPS)
Acute Dystonic Reactions

Acute dystonic reactions occur in approximately 1 in 500 patients treated with the usual adult dosages of 30-40 mg/day of metoclopramide. These usually are seen during the first 24-48 hours of treatment with metoclopramide, occur more frequently in pediatric patients and adult patients less than 30 years of age and are even more frequent at the higher doses used in prophylaxis of vomiting due to cancer chemotherapy. These symptoms may include involuntary movements of limbs and facial grimacing, torticollis, oculogyric crisis, rhythmic protrusion of tongue, bulbar type of speech, trismus, or dystonic reactions resembling tetanus. Rarely, dystonic reactions may present as stridor and dyspnea, possibly due to laryngospasm. If these symptoms should occur, immediate treatment by health care professionals should be initiated to treat this condition.

Parkinsonian-like Symptoms

Parkinsonian-like symptoms, including bradykinesia, tremor, cogwheel rigidity, or mask-like facies, have occurred more commonly within the first 6 months after beginning treatment with metoclopramide, but occasionally after longer periods. These symptoms generally subside within 2-3 months following discontinuance of metoclopramide. Patients with preexisting Parkinson's disease should be given pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION cautiously, if at all, since such patients may experience exacerbation of parkinsonian symptoms when taking pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION.

Neuroleptic Malignant Syndrome (NMS)

There have been rare reports of an uncommon but potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) associated with metoclopramide. Clinical manifestations of NMS include hyperthermia, muscle rigidity, altered consciousness, and evidence of autonomic instability (irregular pulse of blood pressure, tachycardia, diaphoresis and cardiac arrhythmias). When these symptoms occur, treatment with pms-METOCLOPRAMIDE

HYDROCHLORIDE INJECTION and other drugs not essential to concurrent therapy should be discontinued immediately. Intensive symptomatic treatment and medical monitoring should be initiated.

Depression

Mental depression has occurred in patients with and without prior history of depression. Symptoms have ranged from mild to severe and have included suicidal ideation and suicide. pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should be given to patients with a prior history of depression only if the expected benefits outweigh the potential risks.

Use in Pregnancy

The safe use of pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION in pregnancy has not been established. Therefore, pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should not be used in pregnant women unless in the opinion of the physician, the expected benefits outweigh the potential risks to the fetus.

Pediatrics

- pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is contraindicated in children less than 1 year of age.
- pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should not be used in children greater than 1 year of age unless the anticipated benefits clearly outweigh potential risks.
- Extrapyramidal symptoms may also occur in children receiving the daily recommended dose of metoclopramide that should not exceed 0.5 mg/kg.

Metoclopramide elevates prolactin levels; the elevation persists during the chronic administration. Tissue culture experiments demonstrate that about one third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is contemplated in a patient with previously detected breast cancer. Even though disturbances such as amenorrhea, galactorrhea, impotence and gynecomastia have been reported with prolactin elevating drugs, the clinical significance of elevated serum prolactin levels is unknown for the most patients. After chronic administration of prolactin stimulating neuroleptic drugs, an increase in mammary neoplasms has been detected in rodents. However, neither epidemiological studies nor clinical studies conducted to date, have shown an association between chronic administration of these drugs and mammary tumorigenesis. The available evidence is considered to be too limited to be conclusive at this time.

PRECAUTIONS

General

The recommended dosage of metoclopramide should usually not be exceeded since a further increase in dosage will not produce a corresponding increase in clinical response.

Patients with Special Diseases and Conditions

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should not be used in patients with extrapyramidal symptoms or epilepsy unless the expected benefits outweigh the risks of increased frequency and severity of extrapyramidal reactions or seizures.

In patients with pheochromocytoma, IV metoclopramide may cause a hypertensive crisis. Administer phentolamine by slow IV injection to control this effect.

Dosage may need to be reduced in patients with impaired hepatic or renal function (see DOSAGE AND ADMINISTRATION).

DRUG INTERACTIONS

Metoclopramide may reduce the absorption of drugs such as digoxin from the stomach, and accelerate the absorption of drugs such as acetaminophen, ethanol, levodopa and tetracyclines from the small bowel.

Anticholinergic drugs antagonize the effects of metoclopramide on gastrointestinal motility. Metoclopramide should not be used in conjunction with neuroleptic or ganglioplegic drugs as potentiation of effects may occur. The sedative effects of metoclopramide may be potentiated by narcotics, sedatives, anxiolytics, and hypnotics.

Caution should be exercised when pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is administered in combination with MAO inhibitor. In an animal study, pretreatment with MAO inhibitor increased the toxicity of intravenous metoclopramide (see TOXICOLOGY).

In patients with pheochromocytoma, IV metoclopramide may cause a hypertensive crisis. Administer phentolamine by slow IV injection to control this effect.

ADVERSE REACTIONS

Drowsiness, fatigue and lassitude occur in approximately 10% of patients at the normal recommended dosage. Less frequent adverse reactions, occurring in approximately 5% of patients are headache, dizziness, insomnia and bowel disturbances. Menstrual disorders and galactorrhea have also been reported.

The more serious adverse reactions associated with the use of metoclopramide are Parkinsonism and/or other extrapyramidal reactions. These consist often of a feeling of restlessness, facial spasms, involuntary movements, and in some cases, muscular twitching, torticollis, trismus, opisthotonos and oculogyric crisis. Dystonic reactions resembling tetanus have been reported. Extrapyramidal side effects appear to occur more frequently at higher than the normal recommended dosage.

In general, the incidence of adverse reactions correlates with the dose and duration of

metoclopramide administration. Tardive dyskinesia, which in some cases appears to be irreversible, has been reported during long-term treatment (over 12 weeks) and following discontinuation of long-term metoclopramide therapy. Therefore, prolonged treatment with pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should be avoided. Tardive dyskinesia is characterized most frequently by involuntary movements of the tongue, face, mouth or jaw, and sometimes by involuntary movements of the trunk and/or extremities.

OVERDOSAGE

The most frequently reported adverse reactions to overdosage are the extrapyramidal reactions described in the preceding section. Management of overdosage consists of close observation and supportive therapy. Extrapyramidal reactions have been effectively controlled by antiparkinson and antihistamine /anticholinergic drugs such as diphenhydramine hydrochloride.

Hemodialysis removes relatively little metoclopramide, probably because of the small amount of the drug in blood relative to tissues. Similarly, continuous ambulatory peritoneal dialysis does not remove significant amounts of the drug. It is unlikely that the dosage would need to be adjusted to compensate for loss through dialysis. Dialysis is not likely to be an effective method of drug removal in overdose situations.

Methemoglobinemia has occurred in premature and full-term neonates who were given overdoses of metoclopramide (1 - 4 mg/kg/day orally, intramuscularly or intravenously for 1 - 3 or more days). Methemoglobinemia has not been reported in neonates treated with 0.5 mg/kg/day in divided doses. Methemoglobinemia can be reversed by the intravenous administration of methylene blue.

For management of a suspected drug overdose, contact your regional poison control centre.

DOSAGE AND ADMINISTRATION

NOTE: EXCEPT FOR PROPHYLAXIS OF CISPLATIN-INDUCED VOMITING DURING ANTI-CANCER THERAPY, THE TOTAL DAILY DOSAGE MUST NOT EXCEED 0.5 mg/kg BODY WEIGHT.

As an Adjunct in the Management of Delayed Gastric Emptying

Adults: When parenteral administration is required, 2 mL (10 mg) IM or IV (slowly) 2 or 3 times daily as needed.

For the Prophylaxis of Cisplatin-Induced Vomiting

Adults: For the patients treated with cisplatin in doses up to and including 100 mg/m^2, pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION may be administered by infusion after dilution (See Intravenous Infusion) in single doses of 1 mg/kg of body weight. For patients treated

with cisplatin doses greater than 100 mg/ m^2, the single recommended dose may be increased to 2 mg/kg body weight administered by infusion.

Infuse slowly over a 15-minute period and repeat the dose every 2 hours for two doses, then every 3 hours for three doses. (When the 2 mg/kg dose is used, the last dose may be omitted).

For the Prophylaxis of Postoperative Vomiting

Adults: Administer 2 mL (10 mg) intramuscularly near the end of surgery. 20 mg may be required if the patient is in the high-risk group (e.g. general anesthesia of 2 hours or more, abdominal or pelvic surgery with visceral manipulation, absence of gastric suction). Dosing may be repeated every 4 to 6 hours.

For Small Bowel Intubations:

Adults: 10 mg by IV route (slowly) preferably at the time when the tip of the tube reaches the pyloric region.

Children: Single dose of 100 mcg/kg IV slowly.

Use in Patients with Renal or Hepatic Impairment:

Since metoclopramide is excreted principally through the kidneys, in those patients whose creatinine clearance is below 40 mL/min., therapy should be initiated at approximately one-half the recommended dosage. Depending upon clinical efficacy and safety considerations, the dosage may be increased or decreased as appropriate.

See OVERDOSAGE section for information regarding dialysis.

Metoclopramide undergoes minimal hepatic metabolism, except for simple conjugation. Its safe use has been described in patients with advanced liver disease whose renal function was normal.

SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

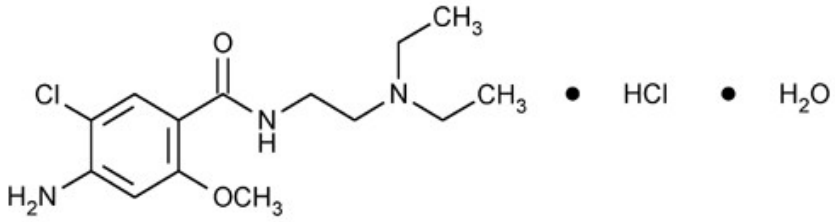
Proper name: Metoclopramide hydrochloride

Chemical name: {4-amino-5-chloro-N-[(2-diethylamino)ethyl]-2-methoxybenzamide}monohydrochloride monohydrate.

Molecular formula: $C_{14}H_{22}ClN_3O_2 \cdot HCl \cdot H_2O$

Molecular mass: 354.27 g/mol

Structural formula:



Physicochemical Properties

Description**:** A white, odourless, crystalline, powder

Solubilities: Very soluble in water, freely soluble in alcohol, sparingly soluble in chloroform; practically insoluble in ether.

The melting point is about 183°C. Metoclopramide hydrochloride has pKas of 0.6 and 9.3. The injection has a pH of 4 to 6.5.

Composition
pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is a sterile solution in single dose glass vials. Each mL of pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION contains metoclopramide hydrochloride 5 mg, sodium chloride 8.5 mg, with water for injection; pH adjusted to 2.5 to 6.5 with hydrochloric acid and/or sodium hydroxide. pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is preservative free.

STORAGE AND STABILITY

Store between 15 and 30ºC. Protect from light. Discard unused portion.

Intravenous Infusion

The 10 mL single use vial containing 50 mg (5 mg/mL) of metoclopramide hydrochloride and the 30 mL single use vial containing 150 mg (5 mg/mL) of metoclopramide hydrochloride are intended for IV infusion after dilution. Dilute the calculated amount of pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION 5 mg/mL with one of the following intravenous solutions:

Dextrose Injection 5%
Sodium Chloride Injection 0.9%
Dextrose 5% in Sodium Chloride 0.45% Injection

Solutions of metoclopramide that have been prepared by dilution of the injection with 50 mL of one of these compatible IV solutions are stable for up to 48 hours when stored at room temperature and exposed to normal light conditions.

Warning: As with all parenteral drug products, IV admixtures should be inspected visually for clarity, particulate matter, precipitate, discolouration and leakage prior to administration, whenever solution and container permit. Solutions showing haziness, particulate matter, precipitate, discolouration or leakage should not be used.

AVAILABILITY OF DOSAGE FORMS

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is available in single use amber glass vials in boxes of 10 x 2 mL, 5 x 10 mL and 1 x 30 mL.

DETAILED PHARMACOLOGY

Metoclopramide is a dopamine antagonist which appears to block preferentially the D-2 (non-adenylate cyclase linked) receptors.

In the rat, metoclopramide antagonizes apomorphine-induced stereotype, causes catalepsy, elevates prolactin, aldosterone and plasma renin levels, and enhances dopamine turnover in mesolimbic and striatal structures.

Metoclopramide antagonizes *in vitro* the dopamine-induced inhibition of potassium-evoked 3H-acetylcholine release in striatal structures. In the rat, parenteral administration of metoclopramide decreases striatal acetylcholine levels. The extrapyramidal side effects caused by metoclopramide and other neuroleptics are believed to be a consequence of this action.

Oral administration of metoclopramide to rats for 39 days induced behavioural supersensitivity to apomorphine and enhanced specific binding of 3H-spiroperidol to striatal membranes. These effects are induced by other neuroleptic drugs, and are associated with a potential to elicit tardive dyskinesia in man.

In experimental animals, metoclopramide enhances gastrointestinal motility, increasing both resting muscle tension and the amplitude of peristaltic movements.

Metoclopramide is virtually inactive as an antagonist at the D-1 (adenylate cyclase linked) dopamine receptors, and is without potency in displacing radiolabelled ligands in receptor models designed to evaluate antipsychotic potential.

In the rat, intraventricular administration of metoclopramide and spiroperidol produce comparable dose-dependent depression of responding in electrical self-stimulation procedures. When administered by the intraperitoneal route, the potency of metoclopramide, but not that of spiroperidol, is decreased by a factor of 30.

TOXICOLOGY

Acute Toxicity

Acute toxicity by the oral route is low in most animal species, though metoclopramide is markedly more toxic when given intravenously. (see table).

Table 1: Acute toxicity of metoclopramide in various animal species

Species	Route of administration	LD_{50} mg/kg
Mouse	Intravenous	63
Mouse	Intramuscular	306
Rat	Intramuscular	325
Rat	Subcutaneous	540
Rat	Intraperitoneal	112

Rat	Oral	401 to 740
Weanling rat	Oral	560
Rabbit	Intravenous	22
Rabbit Oral	Oral	870
Dog	Intravenous	40

Subacute toxicity

Dogs receiving up to 80 mg/kg metoclopramide for 5 days a week over 16 weeks showed marked behavioural changes only at higher doses, characterized by fine tremors, subdued behaviour, anorexia and miosis. These signs disappeared during the weekend withdrawal of the drug.

In studies in rabbits and dogs, animals showed signs of fine tremors, hypoactivity, miosis, panting and bizarre positions following intravenous or intramuscular doses of up to 20 mg/kg metoclopramide for 4 to 5 weeks. These signs appeared and disappeared more rapidly with intravenous than with intramuscular administration, but there were no other signs of drug-related effects and no hematological, biochemical or histopathological changes.

Chronic Toxicity

There were no abnormal hematological, biochemical or histopathological changes in rats receiving daily oral doses of up to 40 mg/kg or 100 mg/kg metoclopramide for 77 weeks or 3 to 6 months respectively. A similar regimen of 300 mg/kg slowed growth and weight gain in some animals, while 600 mg/kg resulted in the death of the majority of animals within the dosage period.

Dogs receiving up to 40 mg/kg daily for 5 days a week showed behavioural changes like those observed in the sub-acute studies, to which tolerance did not develop over 54 weeks. There were no significant alterations in liver, renal or cardiovascular functions, and no hematological, biochemical or histopathological abnormalities.

Teratology and Reproduction Studies

There were no abnormalities or drug-related effects on fetal size and weight, in the offspring of mice, rats and rabbits treated with up to 20 mg/kg metoclopramide daily by the oral, subcutaneous or intravenous routes and at various stages of gestation. Young born to treated animals grew normally, and autopsy at 6 to 10 weeks revealed no abnormalities.

Interaction with Nialamide

Nialamide, a MAO inhibitor, did not potentiate the acute lethality of metoclopramide in rats. These findings contrast with earlier tests showing the phenelzine, another MAO inhibitor, potentiates the acute lethality of metoclopramide in rabbits.

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IMPORTANT: PLEASE READ

CONSUMER INFORMATION

[Pr]pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION

Metoclopramide Hydrochloride Injection, House Standard
Solution for Injection
5 mg / mL of Metoclopramide Hydrochloride

This leaflet is part of a "Product Monograph" published when pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION. Contact your healthcare professional if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is a drug used to treat symptoms of slowed stomach emptying seen in people with gastritis, and in those recovering from certain types of gastric tests or surgery.

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION, when used before surgery, can help reduce vomiting after surgical procedures.

What it does:
pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is a drug used to help speed the movement of food through the stomach and intestines, by stimulating the muscles of the gastrointestinal tract.

When it should not be used:
Do not take pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION if you:

- are allergic (hypersensitive) to metoclopramide or any of the other ingredients listed in "**What the non-medicinal ingredients are."**
- are experiencing bleeding (hemorrhage), a blockage (obstruction), or a tear (perforation) in your stomach or intestines
- metoclopramide should not be used in children less than 1 year of age

What the medicinal ingredient is:
The active substance of pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is metoclopramide hydrochloride.

What the nonmedicinal ingredients are:
The non-medicinal ingredients are: sodium chloride, hydrochloric acid and/or sodium hydroxide and water for injection.

What dosage forms it comes in:
pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is available in single use amber glass vials in boxes of 10 x 2 mL, 5 x 10 mL and 1 x 30 mL.

WARNINGS AND PRECAUTIONS

- **A condition called tardive dyskinesia (see description below) has occurred with long-term (over 12 weeks) use of metoclopramide and even after long-term treatment has been stopped. The chance of this occurring increases with duration of treatment, total cumulative dose and in the elderly, particularly elderly women.**

Children:

- **pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION must not be used in children under 1 year of age**
- **pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should not be used in children over 1 year of age unless the doctor believes the benefit outweighs the risk.**
- **extrapyramidal symptoms (e.g. shaking, tremor, stiffness and involuntary movement) may occur in children. Children's dosage should not exceed 0.5 mg/kg/day.**

Before pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is used, be sure to tell your doctor if you:

- have a history of bleeding (hemorrhage), a blockage (obstruction), or a tear (perforation) in your stomach or intestines
- have a history of seizures (e.g. epilepsy)
- are pregnant. pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION should not be administered in pregnancy unless your doctor believes the benefit outweighs the risk to the fetus.
- are breastfeeding. Metoclopramide can pass into the breast milk and harm your baby. Talk to your doctor about the best way to feed your baby if you receive metoclopramide
- have ever been diagnosed with breast cancer

- have kidney problems
- have an adrenal gland tumour called pheochromocytoma

Contact your doctor immediately if the following occur while receiving metoclopramide:

- You develop symptoms of tardive dyskinesia or dystonia with symptoms such as involuntary movement of lips, eyes, tongue, face, head and limbs.
- You develop Parkinson's symptoms such as tremor, restlessness, muscle rigidity, facial spasms, involuntary movements, and difficulty completing daily tasks.
- You develop symptoms of neuroleptic malignant syndrome with symptoms such as high temperature, muscle rigidity, irregular or fast heartbeat.
- You feel depressed or have thoughts about hurting or killing yourself.

INTERACTIONS WITH THIS MEDICATION

Some medications may block the effects of pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION, such as anticholinergic drugs.

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION may intensify the effect of alcohol and drugs absorbed from the intestines, such as neuroleptics.

Interactions may occur with monoamine oxidase inhibitors (e.g. some drugs used to treat depression).

Some drugs may increase the risk of drowsiness with pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION, such as sedatives, hypnotics, narcotics, and anxiolytics.

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION may decrease the absorption of drugs from the stomach (e.g. digoxin) whereas absorption from the small bowel may be accelerated (e.g. acetaminophen, tetracyclines, levodopa, alcohol).

PROPER USE OF THIS MEDICATION

Usual dose:

Note: **The total adult and pediatric daily dosage must not exceed 0.5 mg/kg/body weight.**

Depending how well you respond to treatment and safety considerations, your dosage of pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION may be increased or decreased by your doctor, as appropriate.

Overdose:

If you think you have taken too much pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION, contact your health care professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

The missed dose should be administered as soon as possible, except if it is almost time for your next scheduled dose. In this case the missed does should be skipped.

Extra medicine should not be administered to make up the missed dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Common side effects

The most common side effects are drowsiness and fatigue.

Other possible common side effects include insomnia, headache, dizziness and bowel disturbances.

If any of these affects you severely, **tell your doctor**.

If you notice any other side effects not mentioned in this leaflet, please inform your healthcare professional.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
Rare	Muscular twitching		√	
	Restlessness		√	
	Facial Spasms or movements		√	
	Unusual eye movements		√	
	Involuntary or unusual movements		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
Rare	Muscle rigidity		√	
	Tremors		√	
	High temperature, fast or irregular heartbeat		√	
	Feeling depressed or thoughts about hurting or killing yourself		√	
	Hypersensitivity (allergic) reaction with symptoms such as rash, hives, breathing difficulty, swelling of the mouth, throat and extremities		√	

This is not a complete list of side effects. For any unexpected effects while taking pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION, contact your healthcare professional.

HOW TO STORE IT

pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION is stored between 15 and 30ºC, protected from light. Unused portion should be discarded. Keep out of reach and sight of children.

Solutions of metoclopramide that have been prepared by dilution of the injection are stable for up to 48 hours when stored at room temperature and exposed to normal light conditions.

As with all parenteral drug products, IV admixtures should be inspected visually for clarity, particulate matter, precipitate, discolouration and leakage prior to administration, whenever solution and container permit. Solutions showing haziness, particulate matter, precipitate, discolouration or leakage should not be used.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

If you want more information about pms-METOCLOPRAMIDE HYDROCHLORIDE INJECTION:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Consumer Information by visiting the Health Canada website (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp); or by contacting the manufacturer, Pharmascience Inc., at 1-888-550-6060.

This leaflet was prepared by:
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