

Data Sheet

MAXOLON

Metoclopramide hydrochloride

Presentation

Maxolon Tablet: White, round, biconvex tablet embossed 'MAXOLON' on one side with a bisecting line on the other. Approximately 7mm in diameter.

This product is not able to deliver all approved dose regimens.

Uses

Actions

Maxolon stimulates motility of the upper gastrointestinal tract without stimulating gastric, biliary, or pancreatic secretions. Its mode of action is unclear. It seems to sensitise tissues to the action of acetylcholine. The effect of Maxolon on motility is not dependent on intact vagal innervation, but it can be abolished by anticholinergic drugs.

Maxolon increases the tone and amplitude of gastric (especially antral) contractions, relaxes the pyloric sphincter and the duodenal bulb, and increases peristalsis of the duodenum and jejunum resulting in accelerated gastric emptying and intestinal transit. It increases the resting tone of the lower oesophageal sphincter. It has little, if any effect on the motility of the colon or gall bladder.

Maxolon has dopamine antagonist activity. Like the phenothiazines and related drugs, which are also dopamine antagonists, Maxolon produces sedation and may produce extra-pyramidal reactions (see Precautions). Maxolon inhibits the central and peripheral effects of apomorphine, induces release of prolactin and causes a transient increase in circulating aldosterone levels.

Pharmacokinetics

The onset of pharmacological action is 1 to 3 minutes following an intravenous dose, 10 to 15 minutes following intramuscular administration, and 30 to 60 minutes following an oral dose; pharmacological effects persist for 1 to 2 hours.

There is marked variability in peak plasma concentrations of Maxolon after oral administration, which appears to be due to interindividual differences in

first-pass metabolism. Plasma protein binding is 13 to 22%. About 80% of the drug is excreted in the urine in the first 24 hours, approximately half as the glucuronide and sulfate conjugates and half as unchanged drug. Elimination half-life varies in different studies from 2.5 to 5 hours. Impaired renal function results in reduced clearance of Maxolon and an increased half-life (15 hours).

Indications

ADULTS (20 years and over)

Digestive Disorders

Maxolon restores normal co-ordination and tone to the upper digestive tract and relieves symptoms of gastroduodenal dysfunction including:

- Dyspepsia
- Heartburn
- Flatulence
- Sickness
- Regurgitation of bile
- Pain.

These symptoms may be associated with such conditions as:

- Peptic ulcer
- Duodenitis
- Reflux oesophagitis
- Gastritis
- Hiatus hernia
- Cholelithiasis and post-cholecystectomy dyspepsia.

Nausea and Vomiting

Maxolon is indicated in the treatment of nausea and vomiting associated with:

- Gastrointestinal disorders
- Cyclical vomiting
- Intolerance to cytotoxic medicines
- Congestive heart failure
- Deep x-ray or cobalt therapy
- Post-anaesthetic vomiting.

Migraine

Maxolon 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 antimigraine therapy (e.g. paracetamol) which may otherwise be impaired in such patients.

Post-Operative Conditions

- Post-operative gastric hypotonia
- Post-vagotomy syndrome.

Maxolon promotes normal gastric emptying and restores motility in vagotomised patients, and where postoperative symptoms suggest gastroduodenal dysfunction.

Diagnostic Procedures

- Radiology
- Duodenal intubation.

Maxolon speeds up the passage of a barium meal by decreasing gastric emptying time, co-ordinating peristalsis and dilating the duodenal bulb.

Maxolon also facilitates duodenal intubation procedures.

YOUNG ADULTS AND CHILDREN

The use of MAXOLON in patients under 20 years should be restricted to the following:

- Severe intractable vomiting of known cause
- Vomiting associated with radiotherapy and intolerance to cytotoxic medicines
- As an aid to gastrointestinal intubation
- As part of the premedication before surgical procedures.

Dosage and Administration

This product is not able to deliver all approved dose regimens.

The dosage recommendations given below should be strictly adhered to if side effects of the dystonic type are to be avoided. It should be noted that total daily dosage of MAXOLON, especially for children and young adults, should not normally exceed 0.5 mg/kg body weight. In patients with clinically significant degrees of renal or hepatic impairment, therapy should be at reduced dosage. Metoclopramide is metabolised in the liver and the predominant route of elimination of metoclopramide and its metabolites is via the kidney.

Medical Indications

Oral

Adults (20 years and older)

10mg three times daily.

For patients less than 60kg, see Table 1.

Elderly patients (as for adults)

To avoid adverse reactions adhere strictly to dosage recommendations and where prolonged therapy is considered necessary, patients should be regularly reviewed.

Young Adults and Children

Maxolon should only be used after careful examination to avoid masking an underlying disorder e.g. cerebral irritation. In the treatment of this group attention should be given primarily to body weight and treatment should begin at the lower dosage where stated.

Tablets should not be used in children under the age of 15.

Table 1			
Young Adults:	15 - 19 years	60kg & over	10mg three times daily
		30kg - 59kg	5mg three times daily
Children:	9 - 14 years	30kg & over	5mg three times daily
	5 - 9 years	20kg - 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 Maxolon may be given 5-10 minutes before the examination. Subject to body weight considerations (see above) the following dosages are recommended:

Table 2		
Adults:	20 years and over	10mg - 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

Contraindications

Maxolon should not be used whenever stimulation of gastrointestinal motility might be dangerous, eg. in the presence of gastrointestinal haemorrhage, mechanical obstruction, or perforation.

Maxolon is contra-indicated in patients with phaeochromocytoma because the drug may cause a hypertensive crisis, probably due to release of catecholamines from the tumour. Such hypertensive crises may be controlled by phentolamine.

Maxolon is contra-indicated in patients with known hypersensitivity or intolerance to the drug.

Warnings and Precautions

Dystonic reactions occur in approximately 1% of patients given Maxolon. These occur more frequently in children and young adults and may occur after a single dose.

Persistent tardive dyskinesia - Tardive dyskinesia may appear in some patients on long-term therapy or may appear after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high dose therapy, especially females. The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterised by rhythmical involuntary movement of the tongue, face, mouth or jaw (eg. protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movement of extremities. There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. If these symptoms appear, it is suggested that the dosage of all antipsychotic or other antidopaminergic agents be progressively reduced with a view to discontinuation if possible. Should it be necessary to reinstitute treatment or increase the dosage of the agent, or switch to a different antidopaminergic agent, the syndrome may be masked. It has been suggested that fine vermicular movements of the tongue may be an early sign of the syndrome, and, if the medication is stopped at that time, the syndrome may not develop.

Care should be exercised in patients being treated with other centrally active drugs.

Since extrapyramidal symptoms may occur with both Maxolon and neuroleptics such as phenothiazines, care should be exercised in the event of both drugs being prescribed concurrently.

Neuroleptic Malignant Syndrome has been reported with Maxolon in combination with neuroleptics as well as with Maxolon monotherapy (see Adverse Effects).

Maxolon elevates prolactin levels and the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of Maxolon is contemplated in a patient with previously detected breast cancer. Although disturbances such as galactorrhoea, amenorrhoea, gynaecomastia, and impotence have been reported with prolactin elevating drugs, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of prolactin stimulating neuroleptic drugs. Neither clinical studies nor epidemiological studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is too limited to be conclusive at this time.

The frequency and severity of seizures or extrapyramidal reactions may be increased in epileptic patients given Maxolon.

Following operations such as pyloroplasty or gut anastomosis, Maxolon therapy should be withheld for three or four days as vigorous muscular contractions may not help healing.

Special care should be taken in cases of severe renal insufficiency (see Dosage and Administration).

The symptomatic relief provided by Maxolon may delay recognition of serious disease. It should not be prescribed until diagnosis has been established, and should not be substituted for appropriate investigation of the patient's symptoms.

Maxolon should not be given to children unless a clear indication has been established for its use, because of the higher incidence of adverse reactions in this age group.

If vomiting persists in a patient receiving Maxolon, the patient should be reassessed to exclude the possibility of an underlying disorder eg. cerebral irritation.

Patients should be cautioned about engaging in activities requiring mental alertness for a few hours after the drug has been administered.

Use in Pregnancy

Category A. Adequate human data on use during pregnancy are not available.

Use in Lactation

Adequate human data on use during lactation and adequate animal reproduction studies are not available.

Adverse Effects

The most frequent adverse reactions to Maxolon are restlessness, drowsiness, fatigue and lassitude, which occur in approximately 10% of patients.

Less frequently, insomnia, headache, dizziness, nausea, or bowel disturbances may occur. Rare (less than 1 in 1,000) cases of acute depression have been reported. Anxiety or agitation may occur.

A single instance of supraventricular tachycardia following intramuscular administration has been reported. There have been very rare (less than 1 in 10,000) cases of abnormalities of cardiac conduction (such as bradycardia and heart block) in association with intravenous metoclopramide.

Raised serum prolactin levels have been observed during Maxolon therapy: this effect is similar to that noted with many other compounds.

Although uncommon at normal dosage, various extrapyramidal reactions to Maxolon, usually of the dystonic type, have been reported. Reactions include: spasm of the facial muscles, trismus, rhythmic protrusion of the tongue, a bulbar type of speech, spasm of the extraocular muscles including oculogyric crises, unnatural positioning of the head and shoulders and opisthotonos. There may be a generalised increase in muscle tone. The majority of reactions occur within 36 hours of starting treatment and the effects usually disappear within 24 hours of withdrawal of the drug, however, close observation is required and in cases of more severe reactions, an antiparkinson drug such as benztropine or an anticholinergic antihistamine such as diphenhydramine should be given.

Tardive dyskinesia, which may be persistent, has been reported particularly in elderly patients undergoing long-term therapy with Maxolon.

Very rare (less than 1 in 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 CPK and must be treated urgently (recognised treatments include dantrolene and bromocriptine). Maxolon should be stopped immediately if this syndrome occurs.

Methaemoglobinaemia has also been reported.

Interactions

The effects of Maxolon on gastrointestinal motility are antagonised by anticholinergic drugs and narcotic analgesics. Additive sedative effects can occur when Maxolon is given with alcohol, sedatives, hypnotics, narcotics or tranquillisers.

Since Maxolon accelerates abnormally slow gastric and small bowel peristaltic activity, it may change absorption of orally administered drugs. The absorption of drugs from the small bowel may be accelerated (eg. paracetamol, tetracycline, L-dopa), whereas absorption of drugs from the stomach may be diminished (eg. digoxin).

Compatibility: If the standard formulation of Maxolon is used for the treatment of nausea and vomiting associated with cytotoxic drugs, the cytotoxic agent should be administered as a separate infusion.

Overdosage

Contact the Poisons Information Centre for advice on the management of overdosage. Extrapyramidal side effects are the most frequently reported adverse reactions to overdosage. Very rarely AV block has been observed. Management of overdosage consists of close observation and supportive therapy. Antiparkinson and antihistamine/anticholinergic drugs such as diphenhydramine hydrochloride have effectively controlled extrapyramidal reactions. Haemodialysis appears ineffective in removing metoclopramide. Similarly, continuous ambulatory peritoneal dialysis does not remove significant amounts of the drug.

Pharmaceutical Precautions

Maxolon Tablet

Tablets should be stored at a temperature not exceeding 30°C. Protect from light.

Medicine Classification

Prescription Medicine

Package Quantities

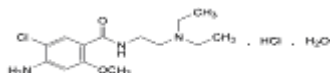
Maxolon Tablet

Packs of 100 (marketed)

Further Information

Composition

Metoclopramide hydrochloride.



$C_{14}H_{22}ClN_3O_2$, HCl, H_2O

CAS number: 54143 -57-6

Description

Chemical name: N-(diethyl-aminoethyl)-2-methoxy-4-amino-5-chlorobenzamide monohydrochloride monohydrate.

List of Excipients

Maxolon tablets also contain the excipients lactose, magnesium stearate, silica - colloidal anhydrous, starch - maize and starch - pregelatinised maize.

Name and Address

Valeant Pharmaceuticals New Zealand Ltd
C/O Supply Chain Solutions
74 Westney Road
Airport Oaks
AUCKLAND

Telephone: 09-257-0521

Date of Preparation

4 June 2010