Metoclopramide

CAS Number : 364-62-5
Molecular Weight : 299.79 g/mol
Molecular Formula : C_{14}H_{22}ClN_{3}O_{2}
Systematic (IUPAC) : 4-amino-5-chloro-N-[2-(diethylamino)ethyl]-2-methoxybenzamide

Type : small molecule
**Description**
A dopamine D2 antagonist that is used as an antiemetic.

**Categories**
Antiemetics
Dopamine Antagonists
Prokinetic Agents

**Taxonomy**

**Kingdom**: Organic

**Classes**
Phenols and Derivatives
  Ethers
  Anisoles
  Benzoyl Derivatives
  Benzamides

**Substructures**
Phenols and Derivatives
  Amino Ketones
  Aliphatic and Aryl Amines
  Ethers
  Benzene and Derivatives
  Aryl Halides
  Carboxylic Acids and Derivatives
  Halobenzenes
  Aromatic compounds
  Anisoles
  Carboxamides and Derivatives
  Benzoyl Derivatives
Pharmacology

**Indication**: For the treatment of gastroesophageal reflux disease (GERD). It is also used in treating nausea and vomiting, and to increase gastric emptying.

**Pharmacodynamics**: Metoclopramide, although chemically related to procainamide, does not possess local anesthetic or antiarrhythmic properties. Metoclopramide is used to enhance GI motility, to treat diabetic gastroparesis, as an antinauseant, and to facilitate intubation of the small bowel during radiologic examination. Metoclopramide may be used to treat chemotherapy-induced emesis and as a radiosensitizing agent in the treatment of non-small cell lung carcinoma and glioblastomas in the future.

**Mechanism of action**: Metoclopramide inhibits gastric smooth muscle relaxation produced by dopamine, therefore increasing cholinergic response of the gastrointestinal smooth muscle. It accelerates intestinal transit and gastric emptying by preventing relaxation of gastric body and increasing the phasic activity of antrum. Simultaneously, this action is accompanied by relaxation of the upper small intestine, resulting in an improved coordination between the body and antrum of the stomach and the upper small intestine. Metoclopramide also decreases reflux into the
esophagus by increasing the resting pressure of the lower esophageal sphincter and improves acid clearance from the esophagus by increasing amplitude of esophageal peristaltic contractions. Metoclopramide's dopamine antagonist action raises the threshold of activity in the chemoreceptor trigger zone and decreases the input from afferent visceral nerves. Studies have also shown that high doses of metoclopramide can antagonize 5-hydroxytryptamine (5-HT) receptors in the peripheral nervous system in animals.

Absorption: Rapidly and well absorbed (oral bioavailability 80±15.5%).

Volume of distribution: 4.4±0.65 L/kg

Protein binding: 30%

Metabolism: Hepatic

Route of elimination: Approximately 85% of the radioactivity of an orally administered dose appears in the urine within 72 hours.

Half life: 5-6 hr

Clearance: 0.67 +/- 0.14 L/hr/kg [infants (0.9-5.4 months) with gastroesophageal reflux (GER)]
Toxicity: Oral, mouse LD50: 280 mg/kg. Signs of overdose include drowsiness, disorientation, and extrapyramidal reactions.

Affected organisms: Humans and other mammals

What is metoclopramide?
Metoclopramide increases muscle contractions in the upper digestive tract. This speeds up the rate at which the stomach empties into the intestines. Metoclopramide is used short-term to treat heartburn caused by gastroesophageal reflux in people who have used other medications without relief of symptoms. Metoclopramide is also used to treat slow gastric emptying in people with diabetes (also called diabetic gastroparesis), which can cause nausea, vomiting, heartburn, loss of appetite, and a feeling of fullness after meals.
Metoclopramide may also be used for purposes not listed in this medication guide.

Drug Class And Mechanisms
Metoclopramide is a "prokinetic" drug that stimulates the muscles of the gastrointestinal tract including the muscles of the lower esophageal sphincter, stomach, and small intestine by interacting with receptors for acetylcholine and dopamine on gastrointestinal muscles and nerves.
The lower esophageal sphincter, located between the esophagus and the stomach, normally prevents reflux of acid and other contents in the stomach from backing up into the esophagus. In patients with gastroesophageal reflux disease (GERD), a weakened lower esophageal
sphincter allows reflux of stomach acid into the esophagus, causing heartburn and damage to the esophagus (esophagitis). Metoclopramide decreases the reflux of stomach acid by strengthening the muscle of the lower esophageal sphincter. Metoclopramide also stimulates the muscles of the stomach and thereby hastens emptying of solid and liquid meals from the stomach and into the intestines.

In some patients, particularly those with diabetes, damage to nerves in the stomach can interfere with function of the muscles and cause delayed emptying of the stomach, resulting in nausea, vomiting, a sense of abdominal fullness and distention, and heartburn (diabetic gastroparesis). Metoclopramide can be effective in relieving the symptoms related to diabetic gastroparesis by stimulating more rapid emptying of the stomach as well as decreasing the reflux of stomach acid into the esophagus. Dopamine receptors on nerves in the brain are important in producing nausea. Metoclopramide interacts with the dopamine receptors in the brain and can be effective in treating nausea. The FDA approved metoclopramide in June 1985.

**Dosing**

The usual dose of metoclopramide for treating GERD is 10-15 mg four times daily, 30 minutes before each meal. Gastroparesis is treated with 10 mg administered orally four times daily, 30 minutes before each meal and at bedtime.

**Drug Interactions**

Since metoclopramide accelerates emptying of the stomach, it can increase or decrease absorption and
effects of other drugs that are absorbed in the small intestine. For example, the effects of alcohol, diazepam (Valium) and cyclosporine can be accelerated when used together with metoclopramide. Conversely, metoclopramide may decrease the concentrations in blood of digoxin (Lanoxin) and cimetidine (Tagamet). Metoclopramide should not be used in patients taking MAO inhibitors for example, isocarboxazid (Marplan), phenelzine (Nardil), tranylcypromine (Parnate), selegiline (Eldepryl), and procarbazine (Matulane), because of the risk of serious adverse effects due to excess release of neurotransmitters. Concurrent administration of anticholinergic drugs can decrease the effectiveness of metoclopramide.

**Why is this medication prescribed?**
Metoclopramide is used to relieve heartburn and speed the healing of ulcers and sores in the esophagus (tube that connects the mouth to the stomach) in people who have gastroesophageal reflux disease (GERD; condition in which backward flow of acid from the stomach causes heartburn and injury of the esophagus) that did not get better with other treatments. Metoclopramide is also used to relieve symptoms caused by slow stomach emptying in people who have diabetes. These symptoms include nausea, vomiting, heartburn, loss of appetite, and feeling of fullness that lasts long after meals. Metoclopramide is in a class of medications called prokinetic agents. It works by speeding the movement of food through the stomach and intestines.
How should this medicine be used?

Metoclopramide comes as a tablet, an orally disintegrating (dissolving) tablet, and a solution (liquid) to take by mouth. It is usually taken 4 times a day on an empty stomach, 30 minutes before each meal and at bedtime. When metoclopramide is used to treat symptoms of GERD, it may be taken less frequently, especially if symptoms only occur at certain times of day.

Follow the directions on your prescription label carefully, and ask your doctor or pharmacist to explain any part you do not understand. Take metoclopramide exactly as directed. Do not take more or less of it or take it more often than prescribed by your doctor.

If you are taking the orally disintegrating tablet, use dry hands to remove the tablet from the package just before you take your dose. If the tablet breaks or crumbles, throw it away and remove a new tablet from the package. Gently remove the tablet and immediately place it on the top of your tongue. The tablet will usually dissolve in about one minute and can be swallowed with saliva.

If you are taking metoclopramide to treat the symptoms of slow stomach emptying caused by diabetes, you should know that your symptoms will not improve all at once. You may notice that your nausea improves early in your treatment and continues to improve over the next 3 weeks. Your vomiting and loss of appetite may also improve early in your treatment, but it may take longer for your feeling of fullness to go away.

Continue to take metoclopramide even if you feel well. Do not stop taking metoclopramide without talking to your doctor. You may experience withdrawal symptoms such as dizziness, nervousness, and headaches when you stop taking metoclopramide.
Other uses for this medicine
Metoclopramide is also sometimes used to treat the symptoms of slowed stomach emptying in people who are recovering from certain types of surgery, and to prevent nausea and vomiting in people who are being treated with chemotherapy for cancer. Ask your doctor about the risks of using this medication to treat your condition.
This medication may be prescribed for other uses; ask your doctor or pharmacist for more information.

What special precautions should I follow?
Before taking metoclopramide, tell your doctor and pharmacist if you are allergic to metoclopramide, any other medications, or any of the ingredients in metoclopramide tablets or solution. Ask your doctor or pharmacist or check the Medication Guide for a list of the ingredients.

Tell your doctor and pharmacist what prescription and nonprescription medications, vitamins, nutritional supplements and herbal products you are taking or plan to take. Be sure to mention any of the following:
acetaminophen (Tylenol, others); antihistamines; aspirin; atropine (in Lonox, in Lomotil); cyclosporine (Gengraf, Neoral, Sandimmune); barbiturates such as pentobarbital (Nembutal), phenobarbital (Luminal), and secobarbital (Seconal); digoxin (Lanoxicaps, Lanoxin); haloperidol (Haldol); insulin; ipratropium (Atrovent); lithium (Eskalith, Lithobid); levodopa (in Sinemet, in Stalevo); medications for anxiety, blood pressure, irritable bowel disease, motion sickness, nausea, Parkinson's disease, ulcers, or urinary problems; monoamine oxidase (MAO) inhibitors, including
isocarboxazid (Marplan), phenelzine (Nardil), selegiline (Eldepryl, Emsam, Zelapar), and tranylcypromine (Parnate); narcotic medications for pain; sedatives; sleeping pills; tetracycline (Bristacycline, Sumycin); or tranquilizers. Your doctor may need to change the doses of your medications or monitor you more carefully for side effects.

tell your doctor if you have or have ever had blockage, bleeding, or a tear in your stomach or intestines; pheochromocytoma (tumor on a small gland near the kidneys); or seizures. Your doctor will probably tell you not to take metoclopramide.
tell your doctor if you have or have ever had Parkinson's disease (PD; a disorder of the nervous system that causes difficulties with movement, muscle control, and balance); high blood pressure; depression; breast cancer; asthma; glucose-6-phosphate dehydrogenase (G-6PD) deficiency (an inherited blood disorder); NADH cytochrome B5 reductase deficiency (an inherited blood disorder); or heart, liver, or kidney disease.
tell your doctor if you are pregnant, plan to become pregnant, or are breast-feeding. If you become pregnant while taking metoclopramide, call your doctor.
if you are having surgery, including dental surgery, tell the doctor or dentist that you are taking metoclopramide.
you should know that this medication may make you drowsy. Do not drive a car or operate machinery until you know how this medication affects you.
ask your doctor about the safe use of alcohol while you are taking this medication. Alcohol can make the side effects of metoclopramide worse.
What special dietary instructions should I follow?
Unless your doctor tells you otherwise, continue your regular diet.

What should I do if I forget a dose?
Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

What side effects can this medication cause?
Metoclopramide may cause side effects. Tell your doctor if any of these symptoms are severe or do not go away:
- drowsiness
- excessive tiredness
- weakness
- headache
- dizziness
- diarrhea
- nausea
- vomiting
- breast enlargement or discharge
- missed menstrual period
- decreased sexual ability
- frequent urination
- inability to control urination

Some side effects can be serious. Call your doctor immediately:
- tightening of the muscles, especially in the jaw or neck
- speech problems
- depression
- thinking about harming or killing yourself
fever
muscle stiffness
confusion
fast, slow, or irregular heartbeat
sweating
restlessness
nervousness or jitteriness
agitation
difficulty falling asleep or staying asleep
pacing
foot tapping
slow or stiff movements
blank facial expression
uncontrollable shaking of a part of the body
difficulty keeping your balance
rash
hives
swelling of the eyes, face, lips, tongue, mouth, throat, arms, hands, feet, ankles, or lower legs
sudden weight gain
difficulty breathing or swallowing
high-pitched sounds while breathing
vision problems

Metoclopramide may cause other side effects. Call your doctor if you have any unusual problems while you are taking this medication.

**What storage conditions are needed for this medicine?**
Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom). Throw away any medication that
is outdated or no longer needed. Talk to your pharmacist about the proper disposal of your medication.

**Symptoms of overdose may include**
- drowsiness
- confusion
- seizures
- unusual, uncontrollable movements
- lack of energy
- bluish coloring of the skin
- headache
- shortness of breath

**What other information should I know?**
- Keep all appointments with your doctor.
- Do not let anyone else take your medication. Ask your pharmacist any questions you have about refilling your prescription.
- It is important for you to keep a written list of all of the prescription and nonprescription (over-the-counter) medicines you are taking, as well as any products such as vitamins, minerals, or other dietary supplements. You should bring this list with you each time you visit a doctor or if you are admitted to a hospital. It is also important information to carry with you in case of emergencies.

**Important information about metoclopramide**
- Never Take metoclopramide In Large Amount Than Recommended, Or For longer Than 2 Weeks
- High doses or long-term use of metoclopramide can cause a serious movement disorder that may not be reversible. Symptoms of this disorder include
uncontrollable muscle movements of your lips, tongue, eyes, face, arms, or legs. The longer you take metoclopramide, the more likely you are to develop a serious movement disorder. The risk of this side effect is higher in women, diabetics, and older adults.

You should not take this medication if you are allergic to metoclopramide, or if you have bleeding or blockage in your stomach or intestines, epilepsy or other seizure disorder, or an adrenal gland tumor (pheochromocytoma).

Before you take metoclopramide, tell your doctor if you have kidney or liver disease, congestive heart failure, high blood pressure, diabetes, Parkinson's disease, or a history of depression.

Do not drink alcohol. It can increase some of the side effects of metoclopramide.

There are many other medicines that can interact with metoclopramide. Tell your doctor about all medications you use. This includes prescription, over-the-counter, vitamin, and herbal products. Do not start a new medication without telling your doctor. Keep a list of all your medicines and show it to any healthcare provider who treats you.

Stop using metoclopramide and call your doctor at once if you have tremors or uncontrolled muscle movements, fever, stiff muscles, confusion, sweating, fast or uneven heartbeats, rapid breathing, depressed mood, thoughts of suicide or hurting yourself, hallucinations, anxiety, agitation, seizure, or jaundice (yellowing of your skin or eyes).
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