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PHARM PROFILE

METOCLOPRAMIDE

- **Manages gastric motility disorders**
- **Manages gastroesophageal reflux**
- **Facilitates intubation of the small intestine**
- **Treats or prevents nausea and vomiting**

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Metoclopramide is a substituted benzamide that is a dopamine-receptor antagonist, an antiemetic, and a gastroprokinetic agent; the drug is not approved for veterinary use in the United States.[1]

PHARMACOLOGY

The antiemetic effect is mediated through antagonism of dopaminergic D_2 receptors centrally and peripherally.[2] The prokinetic effect is mediated through agonism of serotonergic 5-HT_4 receptors.[3] Metoclopramide primarily affects the gastrointestinal (GI) tract in dogs, cats, foals, sheep, cattle, rabbits, and rodents as well as the central nervous system (CNS) in dogs.[4] In the upper GI tract, metoclopramide increases acetylcholine release and the sensitivity of the cholinergic receptors to acetylcholine. This relieves GI motility disorders because inadequate cholinergic stimulation is the cause of most motility impairment.[4] Metoclopramide is also a dopamine antagonist, which is beneficial in the GI tract because dopamine inhibits motility. It stimulates and coordinates esophageal, gastric, pyloric, and duodenal motor activity; increases lower esophageal sphincter tone; and stimulates gastric contractions. In addition, metoclopramide relaxes the pylorus and duodenum, resulting in accelerated gastric emptying and reduced esophageal reflux.[4] It increases duodenal and jejunal peristalsis, resulting in a reduced transit time of ingested material through the intestine. However, metoclopramide has little or no effect on colon motility, making it ineffective in treating colonic disorders, such as constipation and megacolon. In the CNS, metoclopramide readily crosses the blood–brain barrier, where dopamine antagonism at the chemoreceptor trigger zone produces not only an antiemetic effect but also prolactin secretion, sedation, and extrapyramidal effects.[4]

INDICATIONS

Metoclopramide is used in a variety of GI disorders in cats, dogs, foals, sheep, cattle, rabbits, and rodents.[1,3] It is used for managing gastric motility disorders, including gastric stasis, delayed gastric emptying, postoperative ileus, and intestinal pseudo-obstruction; managing gastroesophageal reflux; and facilitating intubation of the small intestine.[3,4] It is also used as an antiemetic in dogs for treating or preventing nausea and vomiting resulting from surgery, chemotherapy, parvovirus, and uremic gastritis.[1,3]

CAUTIONS

Adverse Drug Reactions

Adverse effects of metoclopramide in veterinary medicine are uncommon at recommended doses. However, with large IV doses, behavior changes (e.g., agitation, disorientation), hyperactivity, abdominal pain, and constipation have been noted.[1,5–7] In ponies, IV infusion of metoclopramide at 0.5 mg/kg/hr produced alternating periods of sedation and excitement.[6] In adult horses, IV administration of doses as low as 0.02 mg/kg has been associated with severe CNS side effects (i.e., alternating periods of sedation and excitement).[6] Also in horses, adverse effects (e.g., sedation, yawning, restlessness, excitement) have been reported with the infusion of metoclopramide at 0.25 mg/kg/hr for 30 minutes on three separate occasions 30 minutes apart.[8] Sweating, pain, excitement, hyperirritability,

Table 1. Metoclopramide Dosage and Administration

Purpose	*Dosage*	*Comments*
Prokinetic		
Dogs	0.2–0.5 mg/kg PO or IV q8h[3,10]	
	0.01–0.02 mg/kg/hr or 1–2 mg/kg/day constant IV infusion[3,4,11]	
	0.2–0.5 mg/kg PO or SC q8h[4]	Give at least 30 min before meals and at bedtime[4]
	0.2–0.4 mg/kg PO q6–8h[7,9,12]	Give at least 30 min before meals[7,9,12]
	1–2 mg/kg/day constant IV infusion[7,9]	
Cats	0.2–0.5 mg/kg PO or IV q8h	
	0.01–0.02 mg/kg/hr or 1–2 mg/kg/day constant IV infusion[3,11]	
	0.2–0.5 mg/kg PO or SC q8h[4]	Give at least 30 min before meals and at bedtime[4]
	0.2–0.4 mg/kg PO q6–8h[9,11,12]	Give at least 30 min before meals[9,11,12]
	1–2 mg/kg/day constant IV infusion[7,9]	
Horses[a]	0.125–0.25 mg/kg IV over 60 min[4]	Dilute in 500 ml of polyionic solution[4]
	0.125 mg/kg saline IV drip for 30–60 min[8,13]	
Foals	0.02–0.2 mg/kg IV or IM tid–qid[6]	Slow IV infusion may be more effective[6]
Sheep and cattle	0.3 mg/kg SC q6–8h[4]	
Rabbits	0.2–1.0 mg/kg PO or SC q6–8h[14]	
Rodents	0.2–1.0 mg/kg PO, SC, or IM q12h[15]	
Antiemetic		
Dogs	0.25–0.5 mg/kg IV q8–12h[5,11]	
	1–2 mg/kg/day constant IV infusion[5,9,12]	Efficacy increases with IV infusion versus intermittent boluses[5,9,12]
	0.2–0.4 mg/kg PO or SC q6–8h[9]	
	0.01–0.02 mg/kg/hr continuous IV infusion[9]	
	0.2–0.4 mg/kg IM or SC q8h[16]	Give IM or SC for emesis with parvoviral infection[16]
	1–2 mg/kg/day continuous IV drip[9,16]	Give IV for severe cases[9,16]

[a]Some authors do not recommend metoclopramide for routine use in adult horses because of its CNS effects.[6]

nervousness, and kicking have been reported with 0.125 mg/kg given in a saline IV drip over 30 to 60 minutes.[13] However, the incidence of these adverse effects in foals appears to be less common.[6] Adverse effects that have been reported in humans and are potentially plausible in animals include extrapyramidal effects, nausea, diarrhea, transient hypertension, hypotension, and elevated prolactin levels.[1]

Contraindications

Metoclopramide is contraindicated in patients with hypersensitivity or intolerance to the drug or its components and in patients with GI obstruction, perforation, or bleeding.[1,2] It is also contraindicated in patients with pheochromocytoma because it can stimulate the release of catecholamines, possibly leading to a hypertensive crisis. Metoclopramide should be used cautiously, if at all, in

patients with seizure disorders because the drug may increase the frequency and severity of seizures and in patients with impaired renal function because the drug may accumulate and cause toxicity.[1,2]

Use in Pregnancy

Metoclopramide is classified as a pregnancy category B drug.[2,10] It is likely to cross the placenta and be excreted in milk. Reproduction studies in mice, rats, and rabbits using doses up to 250 times the usual human dose have not revealed evidence of harm to fetuses. However, there have been no adequate and controlled studies to date, so the drug should be used during pregnancy only when clearly needed.[2,10]

ACUTE TOXICITY

There is no clearly defined relationship between plasma levels of metoclopramide and severity of intoxication.[1,2] The oral LD_{50} of metoclopramide is 465 mg/kg in mice, 760 mg/kg in rats, and 870 mg/kg in rabbits.[1,2] Because the lethal dose is high, death caused by overdose is unlikely. However, the following signs of metoclopramide overdose are common in all species: dyspnea, excessive lacrimation, decreased activity, ataxia, miosis, tachycardia, tremors, and tonic seizures.[1,2]

Treatment of metoclopramide overdose involves supportive care and relief of signs.[1,2] Following acute ingestion, the stomach should be emptied. Gastric lavage should be performed if aspiration of gastric contents can be prevented. There is no specific antidote, but agents with anticholinergic activity, such as diphenhydramine and benztropine, are useful in controlling extrapyramidal effects. Signs are generally self-limiting and usually subside within 24 hours.[1,2]

DRUG INTERACTIONS

Anticholinergic drugs (e.g., atropine) and opioid analgesics block the prokinetic action of metoclopramide.[11] The prokinetic effect may reduce the absorption of drugs that are absorbed in the stomach (e.g., digoxin) and increase the absorption of drugs in the small intestine (e.g., cimetidine).[1] Butyrophenones (e.g., haloperidol) and phenothiazines (e.g., prochlorperazine) should be avoided because they can potentiate adverse CNS effects.[4] In addition, the dose and timing of insulin therapy may need to be modified because metoclopramide alters the rate of insulin absorption.[11]

MONITORING

When using metoclopramide, it is important to monitor for clinical efficacy and adverse effects, such as dystonic or extrapyramidal reactions (e.g., muscle spasms, motor restlessness, inappropriate aggression, irritable confusion). Periodic renal function tests, including serum creatinine and blood urea nitrogen levels, should be monitored as well.[4]

PREPARATIONS

No veterinary preparations of metoclopramide are available, but there are several human preparations.[1,2] The most common product, Reglan (Robins), is available in 5- and 10-mg tablets, 1-mg/ml sugar-free syrup in 480-ml bottles and 10-ml unit dose packages, and 5-mg/ml injections in 2- and 10-ml ampules as well as 2-, 10-, 30-, 50-, and 100-ml vials (with and without preservatives). The 10-mg tablets are also available through various other brand name and generic drug manufacturers.[1,2] Metoclopramide has been evaluated for transdermal administration in dogs, but measurable serum concentrations have not been detected.[17]

See Table 1 for dosage and administration of metoclopramide.

STORAGE AND HANDLING

Metoclopramide should be stored at room temperature and in tightly sealed containers protected from light and freezing.[1,2]

Client Counseling Information[1,2]

- Metoclopramide facilitates the movement of food and liquid through the stomach and intestines. The drug also helps relieve nausea and vomiting after surgery or chemotherapy.
- Metoclopramide works best if your pet receives it 30 minutes before a meal and at the same time each day.
- Contact your veterinarian if your pet develops any adverse effects (e.g., uncontrolled movement of the eyes, face, and/or limbs; rigid posture).

REFERENCES

1. Plumb DC: Metoclopramide. *Veterinary Drug Handbook*, ed 4. Ames, Iowa State University Press, 2002, pp 544–547.
2. AHFS Drug Information: Metoclopramide hydrochloride. Bethesda, MD, American Society of Health-System Pharmacists, 2002, pp 2843– 2849.
3. Hall JA, Washabau RJ: Diagnosis and treatment of gastric motility disorders. *Vet Clin North Am Small Anim Pract* 29:377–395, 1999.
4. Dowling PA: Prokinetic drugs: Metoclopramide and cisapride. *Can Vet J* 36:115–116, 1995.
5. Willard MD: Gastrointestinal drugs. *Vet Clin North Am Small Anim Pract* 28:377–394, 1998.
6. Clark ES, Becht JL: Clinical pharmacology of the gastrointestinal tract. *Vet Clin North Am Equine Pract* 3:101–122, 1987.
7. Davis LE: Metoclopramide. *JAVMA* 183:1341–1343, 1983.
8. Freeman DE: Gastrointestinal pharmacology. *Vet Clin North Am Equine Pract* 3:535–559, 1999.
9. Ettinger SJ, Feldman EC: The gas-

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trointestinal system and chronic renal failure. *Textbook of Veterinary Internal Medicine*, ed 4. Philadelphia, WB Saunders, 1995, pp 1133–1232, 1745–1760.

10. Schulze-Delrieu K: Drug therapy. *N Engl J Med* 305:28–33, 1981.
11. Hall JA, Washabau RJ: Gastrointestinal prokinetic therapy: Dopaminergic antagonist drugs. *Compend Contin Educ Pract Vet* 19:214–221, 1997.
12. Hall JA, Twedt DC, Burrows CF: Gastric motility in dogs, Part II: Disorders of gastric motility. *Compend Contin Educ Pract Vet* 12:1373–1390, 1990.
13. Adams SB: Recognition and management of ileus. *Vet Clin North Am Equine Pract* 4:91–104, 1988.
14. Ivey ES, Morrisey JK: Therapeutics for rabbits. *Vet Clin North Am Exotic Anim Pract* 3:183–220, 2000.
15. Adamcak A, Otten B: Rodent therapeutics. *Vet Clin North Am Exotic Anim Pract* 3:221–237, 2000.
16. Pollock RV, Coyne MJ: Canine parvovirus. *Vet Clin North Am Small Anim Pract* 23:555–568, 1993.
17. Mitchener KL, Ogilvie GK, Wash AM, et al: Pharmacokinetics of oral, subcutaneous, and transdermal metoclopramide in client-owned dogs: A randomized study. *Proc Vet Cancer Soc*: 2001.