ANTIEMETIC DRUGS

* Protracted vomiting is physically exhausting and can cause dehydration, acid-base and electrolyte disturbances, and aspiration pneumonia.
* Antiemetic drugs are used to control excessive vomiting once an etiologic diagnosis has been made, to prevent motion sickness and psychogenic vomiting, and to control emesis from radiation and chemotherapy.
* Antiemetics may act peripherally to reduce afferent input from receptors or to inhibit efferent components of the vomiting reflex response. They may also act centrally to block stimulation of the CTZ and emetic center.

|  |  |  |
| --- | --- | --- |
| http://www.merckmanuals.com/site_images/mm/s.gif | http://www.merckmanuals.com/site_images/mm/s.gif | http://www.merckmanuals.com/site_images/mm/s.gif |
|

|  |
| --- |
| **Antiemetic Drugs** |
| **Drug** | **Dosage** |

|  |  |
| --- | --- |
| Acepromazine | 0.025–0.2 mg/kg, IV, IM, SC, maximum 3 mg; 1–3 mg/kg, PO |
| Chlorpromazine | 0.5 mg/kg, IV, IM, SC, tid-qid |
| Prochlorperazine | 0.1 mg/kg, IM, tid-qid; 1 mg/kg, PO, bid |
| Promethazine | 2 mg/kg, PO or IM, sid |
| Isopropamide | 0.2–1.0 mg/kg, PO, bid |
| Propantheline | 0.25 mg/kg, PO, tid |
| Dimenhydrinate | 4–8 mg/kg, PO, tid |
| Diphenhydramine | 2–4 mg/kg, PO, tid |
| Cyclizine | 4 mg/kg, PO, tid |
| Meclizine | 4 mg/kg, PO, sid |
| Butorphanol | 0.2–0.4 mg/kg, IM, sid-bid |
| Metoclopramide | 0.1–0.5 mg/kg, IM, SC, or PO, tid; 0.01–0.02 mg/kg/hr, IV infusion |
| Ondansetron | 0.1–0.2 mg/kg, PO, sid-bid; 0.1–0.15 mg/kg, IV, bid-tid |
| Granisetron | 0.5–1.0 mg/kg, PO, bid; 0.1–0.15 mg/kg, IV, bid-tid |
| Dolasetron | 0.6–1.0 mg/kg, IV, sid |
| Maropitant | 2 mg/kg, PO or 1 mg/kg, SC, sid for up to 5 days (acute vomiting); 8 mg/kg, PO, sid for up to 2 days (motion sickness) |

 |

* The **phenothiazine tranquilizers** antagonize the CNS stimulatory effects of dopamine, thereby decreasing vomiting from many causes. These drugs also have antihistaminic and weak anticholinergic action. Phenothiazine tranquilizers used as antiemetics include acepromazine, chlorpromazine, and prochlorperazine. Potential side effects include hypotension due to α-adrenergic blockade, excessive sedation, extrapyramidal signs, and a lowering of the seizure threshold in epileptics. Extrapyramidal signs can be counteracted with an antihistamine (such as diphenhydramine).
* The **anticholinergic drugs** block cholinergic afferent pathways from the GI tract and the vestibular system to the vomiting center. Alone, they are less effective than the other emetics. Atropine, scopolamine, and isopropamide cross the blood-brain barrier. They tend to have a brief duration of effect and cause excitement in cats. Peripherally-acting anticholinergic drugs include glycopyrrolate, propantheline, and methscopolamine. Only isopropamide and propantheline are commonly used in small animals for vomiting related to vestibular stimulation (also see [Motion Sickness](http://www.merckmanuals.com/vet/nervous_system/motion_sickness/overview_of_motion_sickness.html)).
* The **antihistamines** can block both cholinergic and histaminic nerve transmission responsible for transmission of the vestibular stimulus to the vomiting center. The histamine (H1)-blocking drugs include diphenhydramine, dimenhydrinate, prometh-azine (a phenothiazine with H1- effects), cyclizine, and meclizine. They may cause mild sedation, especially diphenhydramine, dimenhydrinate, and promethazine. Cyclizine and meclizine are potentially teratogenic at high doses.
* **Metoclopramide** exerts its antiemetic effects via 3 mechanisms. At low doses, it inhibits dopaminergic transmission in the CNS, while at high doses, it inhibits serotonin receptors in the CTZ. Peripherally, metoclopramide increases gastric and upper duodenal emptying. Metoclopramide is a popular antiemetic for small animals. It is used to control emesis induced by chemotherapy, nausea and vomiting associated with delayed gastric emptying, reflux gastritis, and viral enteritis. There is tremendous individual variability in metoclopramide pharmacokinetics, and oral bioavailability is only ∼50% due to a significant first-pass effect. At high doses or with rapid IV administration, metoclopramide causes CNS excitement by dopamine antagonism (similar to the phenothiazine tranquilizers). Extrapyramidal signs can be counteracted with an antihistamine such as diphenhydramine. Metoclopramide should not be administered if a GI obstruction or perforation is suspected.
* The **serotonin antagonists**ondanse-tron, granisetron, and dolasetron are specific inhibitors of serotonin subtype 3 receptors in the CTZ. These receptors are located peripherally on vagal nerve terminals and centrally in the area postrema of the brain. Cytotoxic drugs and radiation damage the GI mucosa, causing release of serotonin. These are the most effective antiemetics used in people undergoing radiation and chemotherapy, and they have been used in cats and dogs receiving chemotherapy. Granisetron is more effective than ondan-setron in the inhibition of cisplatin-induced nausea in dogs. They are not effective for emesis caused by motion sickness. All serotonin subtype 3 antagonists have been associated with QT interval prolongation in humans. Adverse effects of dolasetron include ECG changes (PR and QT prolongation, QRS widening) caused by dolasetron metabolites that block sodium channels.
* **Butorphanol** is an effective antiemetic for dogs receiving cisplatin chemotherapy. It causes only mild sedation. It is believed to exert its antiemetic effect directly on the vomiting center.
* **Maropitant** is a neurokinen 1 (NK-1) receptor antagonist approved to treat and prevent emesis in dogs. Until very recently, only 3 neurotransmitter receptors (dopamine D2, serotonin subtype 3, and cannabinoid-1) were identified targets of currently available antiemetic drugs. It is now established that substance P has a role in emesis. Substance P is a regulatory peptide that binds to the NK-1 receptors, which are found in the gut and the emetic center of the CNS. Substance P induces emesis, and selective substance P antagonists are potent antiemetics with a broader spectrum of activity against a variety of emetic stimuli than the serotonin subtype 3 antagonists. In clinical trials, maropitant blocked apomorphine-, cisplatin-, and syrup of ipecac-induced vomiting.
* For motion sickness, maropitant is given at the high dose sid for up to 2 days in a row, and should be given on a relatively empty stomach 2 hr before travelling, with a small amount of food. For acute vomiting (such as with chemotherapy), it can be given at lower doses either PO or SC.
* Adverse effects are rare; the most common are excessive drooling, lethargy, lack of appetite, and diarrhea. A few dogs may vomit after taking the medicine. Giving maropitant with a small amount of food helps prevent vomiting.