

APETIKAN

Oral Solution

Appetite stimulant that promotes weight gain..

REGISTRATION NUMBER Q-7972-046

FORMULA:

Cyproheptadine..... 200 mg.
 Vit B1 (thiamine)..... 20 mg.
 Vit. B6 (pyridoxine)..... 20 mg.
 Vit. B12 (cyanocobalamin)..... .2.3 mg.
 Vehicle c.b.p.....100 ml.

Presentation: 30 ml bottle solution.

INDICATIONS:

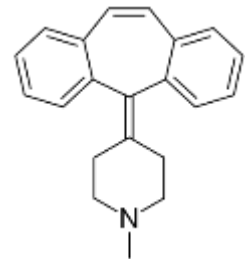
It is an appetite stimulant for puppies and adults who have suffered from bacterial, viral or parasitic diseases, which inhibit appetite, helps early recovery avoiding decompensation in the organism and increasing weight gain. Coadjuvant in postoperative treatment. It is also a serotonin antagonist antihistamine blocker of H1 for the management of pruritus and dermatological allergies in dogs and cats; its vitamin supplement helps in the early recovery of those animals that are weakened.

CYPROHEPTADINE HYDROCHLORIDE:

PROPERTIES AND USES:

It is an orexigen (appetite stimulant), piperidine derivative of dibenzocycloheptene. The appetite stimulant effect is mainly due to its anti-serotonergic action, by antagonizing the 5-HT₂ (S₂) serotonin receptors.

It also has H₁ antihistamine, anticholinergic, and central sedative activity. It can be used in the symptomatic relief of hypersensitization reactions such as urticaria and angioedema, rhinitis, conjunctivitis, and skin alterations with pruritus at high doses. It also has application in prophylaxis and treatment of migraine and vascular headaches, as an appetite stimulant particularly in anorexia nervosa, in cachexia patients with advanced cancer, and in the control of diarrhea associated with carcinoid syndrome.



Mechanism of action: cyproheptadine does not prevent histamine release (like cromoglycate, e.g.) but competes with histamine at H₁ receptors. Cyproheptadine competitively antagonizes the effects of histamine on H₁ receptors in the digestive tract, uterus, large vessels and bronchial smooth muscle. Blockade of H₁ receptors suppresses the formation of edema, pruritus and other reactions resulting from histamine activity. The sedative effects of cyproheptadine are explained by its antagonistic effects at the level of central histaminergic receptors, although the sedation is not as pronounced as with other H₁ antagonists such as diphenhydramine.

Serotonin antagonism in the appetite center of the hypothalamus may explain the ability of cyproheptadine to stimulate appetite.

PHARMACOKINETICS:

The pharmacokinetic characteristics of cyproheptadine indicate good oral absorption and extensive hepatic metabolism generating metabolites with predominant renal excretion. Although the pharmacokinetic characteristics of antihistamines in dogs and cats have not been established, these drugs are rapidly absorbed and reach peak plasma levels within 1 hour of oral administration and the duration of effect is approximately 8



hours. These agents are metabolized in the liver and excreted in the urine. They can cross the placenta and be excreted in milk.

It is metabolized in the liver by hydroxylation and glucuronidation. The main metabolite that appears in the urine is a quaternary ammonium glucuronide. It is excreted by biliary and renal routes. At least 40% of the dose appears in the urine; however, unmodified cyproheptadine is not detected. Between 2 and 20% of the dose appears in fecal matter. Of this amount, only 34% appears untransformed.

Antihistamines are effectively absorbed after oral administration in monogastric animals. In ruminants, they should always be administered parenterally.

When administered orally, pharmacological effects appear 20 to 45 minutes after application. This interval is shortened if they are administered intramuscularly and even immediate effects are obtained if they are applied intravenously. However, the latter route should be considered with caution since signs of nervous stimulation and cardiovascular disorders often appear, especially in cats and horses.

Thiamine is absorbed gastrointestinally and metabolized in the liver. Elimination is renal, mostly in the form of metabolites.

Pyridoxine, pyridoxal and pyridoxamine are rapidly absorbed from the digestive tract after hydrolysis of their phosphorylated derivatives. Pyridoxal phosphate accounts for at least 60% of circulating vitamin B6. Pyridoxal is thought to be the primary form that crosses cell membranes. The major excretion product is 4-pyridoxic acid, formed by the action of hepatic aldehyde oxidase on free pyridoxal.

Once absorbed, vitamin B12 binds to transcobalamin, a plasma β -globulin, for transport to the tissues. Other transcobalamins (I and III), whose concentrations are related to the rate of granulocyte turnover, are also found in plasma. This vitamin is stored as an active coenzyme with a turnover rate of 0.5 to 8 μ g/day depending on the magnitude of the reserves.

PHARMACODYNAMICS:

The structure of cyproheptadine is similar to that of the H1 antagonist phenothiazines and this drug has antiserotonergic (anti 5-HT) activity. Like other H1 antagonists, cyproheptadine competes with histamine for H1 receptors located on effector cells. Cyproheptadine also has potent anti-serotonergic (anti-5-HT) activity because it blocks the 5-HT2A receptor. It also possesses weak anticholinergic and central depressant properties. As local 5-HT levels would be compromised to stimulate CRH and/or ACTH secretion, cyproheptadine could reduce ACTH production in some HDH patients.

Vitamin B1 or thiamine: Converts carbohydrates into energy and keeps nerves, skin and muscles healthy. Important to prevent depression.

Vitamin B6 or Pyridoxine: Muscle stimulant. It helps in the formation of hemoglobin, protects the skin and facilitates growth. Its deficiency causes numerous nervous (depression, insomnia) and muscular diseases, as well as anemia, arteriosclerosis, cramps.

Vitamin B12 or Cyanobalmin: Involved in the formation of red blood cells and integrity of the spinal cord. It is needed for the growth and maintenance of healthy skin and nerves. Its deficiency causes anemia, neuralgia, diabetes, rheumatism, physical fatigue, allergies.

INTERACTIONS WITH OTHER DRUGS

They are not very common in veterinary medicine. CNS depressant drugs such as barbiturates and/or tranquilizers. SSRI drugs include sertraline, fluoxetine, paroxetine, etc. Cyproheptadine can decrease the efficacy of SSRIs.

ROUTE OF ADMINISTRATION: Oral.

DOSE:**Canines:**

As appetite stimulant and antihistamine: 0.15 ml per kg body weight (one drop/kg) (0.3 mg of cyproheptadine per kg body weight), 2 times a day.

Felines:

As appetite stimulant: 1.5 ml per cat (3 mg of cyproheptadine per cat), 2 times a day. As antihistamine: 1 ml per kg of weight (2 mg of cyproheptadine per kg of weight), every 12 hours.

Suggested doses

In dogs for adjuvant treatment of serotonergic syndrome: 1.1 mg / kg PO; Doses can be repeated q4 - 6h as necessary until signs have disappeared. In cases where PO dosing is not possible (severe vomiting), you can crush the tablets and mix with saline solution and give rectally. As an antihistamine although it is one of the most effective it does not always work especially in pruritus so doses are varied ranging from 0.3 - 2 to 4 mg / kg PO twice a day.

In cats it is more functional as an antihistamine and antipruritic so it is suggested 2 mg per PO cat every 12 hours, in the case of feline asthma (especially when cats are heavily medicated with doses of corticosteroids and terbutaline): 2 mg PO every 12 hours. There are times when the response is not as rapid but CNS depression can occur within 24 hours.

For adjuvant treatment of serotonergic syndrome is suggested 2-4 mg (total dose) PO; doses can be repeated every 4 - 6h as needed until signs have disappeared. In cases where PO dosing is not possible (severe vomiting), you can pulverize the tablets and mix with saline and give rectally.

ADVERSE EFFECTS

The most common adverse effects observed with cyproheptadine are related to its CNS depressant effect (sedation) and anticholinergic effects (dryness of mucous membranes, etc.). Cats may develop a paradoxical agitated state that resolves upon dose reduction or discontinuation. Cases of cyproheptadine-induced hemolytic anemia have been reported in cats. Horses may exhibit mild depression, anorexia, or lethargy.

At higher doses, cyproheptadine has caused significant polyphagia in dogs. It has been used 32 times the normal dose in without evidence of adverse effects to the fetus; however, for safety reasons, overdosage during pregnancy has not been recommended.

OVERDOSE AND ACUTE TOXICITY

No specific antidotes are available. In significant overdoses, gastric lavage and bowel emptying and supportive therapy are recommended when necessary. The adverse effects observed with overdose are an extension of the side effects of the drug, mainly CNS depression (although CNS stimulation can be seen), anticholinergic effects (severe drying of mucous membranes, tachycardia, urinary retention, hyperthermia, etc.) and, possibly, hypotension. Physostigmine may be considered for the treatment of severe CNS anticholinergic effects, and diazepam employed to treat seizures, if necessary.

WARNINGS AND/OR RESTRICTIONS:

In dogs it may cause polyphagia, restlessness and excitement. In cats polyphagia, sedation, increased vocalization and vomiting may occur. Not recommended for animals with liver or cardiovascular disease, hypertension, glaucoma, hyperthyroidism or history of seizures, urinary retention or intestinal atony.

Keep in a dry, cool place at no more than 30°C and protected from direct sunlight. Keep out of reach of children, domestic animals and handicapped persons. Any unused veterinary medicinal product, residues derived from it and empty containers should be disposed of safely and in accordance with local regulations, avoiding contamination of water sources. **Product for exclusive use in Veterinary Medicine.**

Consult your veterinarian

Exclusive literature for veterinarians.

Its sale requires medical prescription.

Responsible for content: Technical Department

Bibliography

1. Adams H.R. Veterinary Pharmacology and Therapeutics. 8 th ed. Iowa State University Press, Ames. 2003.
2. Goodman & Gilman. The Pharmacological Basis of Therapeutics. 12th ed. McGrawHill Interamericana, Mexico. 2012.
- Gutierrez T C. UPDATE ON THE NEUROPHYSIOLOGY OF PRURITUS AND THE NEW THERAPEUTIC APPROACH IN THE DOG AND CAT Thesis for the Professional Degree of Veterinary Doctor Department of Clinical Sciences FMV and CP University of Chile SANTIAGO, CHILE 2013.
4. Marin H J Practical Pharmacology in Cats 1st Edition 2016 Celsa impresores
5. Plumb, D. C. (2010). Plumb, Manual de Farmacología Veterinaria. Autonomous City of Buenos Aires, Argentina: Inter-Médica 6th edition.
6. Sumano L.H, Ocampo C.L and Gutiérrez O.L. Farmacología Veterinaria. 4th ed. Diseños e Impresiones Aranda S. A. de C. V. 2015.
7. URL: https://veterinarypartner.vin.com/doc/?id=4952256&pid=19239_382614.1634663152

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