InnoPharma LABORATORIO	**MEDICAL INFORMATION ON VETERINARY PRODUCTS**
	KALMAX Fluoxetine 10 mg /tablet

KALMAX

Registration number Q-0666-049

FORMULA:

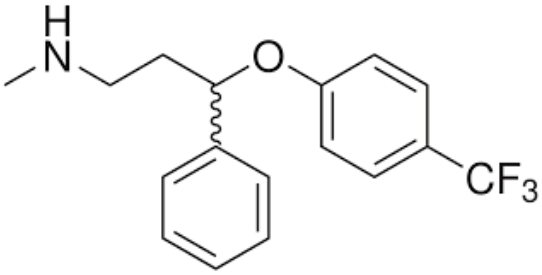
Each tablet contains:
Fluoxetine hydrochloride equivalent to.....10.0 mg
of Fluoxetine
Excipients q.s. ..... tablet

THERAPEUTIC INDICATIONS

Kalmax 10, is a selective serotonin receptor inhibitor, with little sedative effect used as a treatment to control several unwanted behaviors in dogs. Such as cases of aggression, separation anxiety, dominance aggression, licking dermatitis, stereotypies, etc...

PHARMACOLOGY

Fluoxetine is a bicyclic compound that belongs to the family of selective serotonin reuptake inhibitors, it is a solid, crystalline substance, soluble in water and unstable to light. Its chemical formula is (RS)-N-methyl-3-phenyl-3-[4-triflouromethylphenoxy] propylamine hydrochloride (C17H18F3NO HCI), with a molecular weight of 345.8.



Fluoxetine does not act as a sedative, potentiates serotonergic neurotransmission, and produces functional effects due to increased activation of serotonin receptors.
The lack of affinity of fluoxetine for adrenergic, histaminic, muscarinic, opioid, or dopaminergic receptors prevents sedation and anticholinergic properties that produce an increase in serotonergic efficacy. The result is an increase in serotonergic neurotransmission by making serotonin molecules act for a more prolonged period of time. Fluoxetine is shown as a racemic mixture containing R and S enantiomers, 50:50, with potencies comparable to the processes of

absorption 5-HT uptake (Ki ~ 20 nM), since S-norfluoxetine is 14X more potent than R-norfluoxetine with Ki values of 20 and 268 nM, respectively.

With prolonged use, there is a regulated decrease of the neurotransmitter receptors, which improves anxiety states in animals. Its effects are expected from three weeks after administration. It differs chemically and pharmacologically from other antidepressant drugs such as monoamine oxidase inhibitors (MAOIs) or tricyclic antidepressants. Fluoxetine produces beta-adrenoreceptor subsensitization; it does not induce desensitization of serotonergic autoreceptors, but facilitates serotonergic neurotransmission through sensitization of postsynaptic 5-HT1A receptors, as it increases extracellular levels of serotonin by inhibiting its reuptake into the presynaptic neuron, increasing the level of serotonin available to act on the postsynaptic receptor.
It has been described that fluoxetine and fluvoxamine can inhibit dopamine synthesis in some areas of the brain and induce the appearance of extrapyramidal disorders, thus avoiding toxic phenomena such as cardiotoxicity and CNS toxicity of tricyclic antidepressants, due to the selectivity of their mechanism of action. For this reason, it is currently considered the drug of the first choice in modern antidepressant therapy.

PHARMACOKINETICS

Fluoxetine is a very liposoluble molecule that is absorbed in 72% orally, diffusing widely through the body, reaching concentrations between 4 to 8 hours after administration, it has a half-life of 1.8 hrs, while norfluoxetine in average 9.3 hours, it binds strongly to plasma proteins with a maximum plasma concentration of 48.8 ng/ml, for fluoxetine and 70.1 ng / ml for norfluoxetine. It has a bioavailability of 72%, without the presence of food altering its absorption, but it can displace other drugs such as digoxin, salicylates, dicoumarin anticoagulants, and phenothiazines. The volume of distribution (VD) for fluoxetine is 38.9 L / kg, and for norfluoxetine 10.9 L / kg. It is biotransformed in the liver, by N-demethylation forming the metabolite norfluoxetine, subsequently, both products are conjugated with glucuronic acid; They are excreted via the kidneys, giving rise to an active metabolite with a very long plasma half-life (norfluoxetine). Of the total drug recovered in urine, 60% of the dose administered after thirty-five days, 2.5% corresponds to unchanged fluoxetine, 5.2% to fluoxetine glucuronide, and 5.5% to fluoxetine glucuronide, 2% to fluoxetine glucuronic acid, 10% to norfluoxetine and 9.5% to norfluoxetine-glucuronide, while the products corresponding to the remaining 72.8% of the fraction excreted in urine have not been identified. In cats, the elimination half-life of fluoxetine and norfluoxetine is 47-52 hours.

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The fluoxetine derivative, i.e. norfluoxetine, inhibits some cytochrome P450 isoenzymes and can therefore inhibit the biotransformation of many drugs. Since it has a relatively long half-life, its effects take several days to two weeks according to some authors, and up to 6-8 weeks according to others to become evident. The recommended doses would be 1 mg/kg every 24 hours. Since this substance is metabolized in the body, when cases of hepatic dysfunction occur, a dose adjustment will be required.

In male and female dogs treated with doses of 5 to 20 mg/kg fluoxetine for 95 days, the highest concentration of fluoxetine in the liver was followed in decreasing order of concentration by the lung, kidney, various areas of the brain, and plasma. The heart had the lowest levels. Fluoxetine concentrations in these tissues were 50 to 100 times higher than plasma concentrations, in the case of norfluoxetine, the concentrations were 2 to 3 times higher than those of fluoxetine in plasma.
In male and female Beagle dogs treated with fluoxetine at doses of 1 to 10 mg/kg for 1 year, fluoxetine and norfluoxetine dose-dependent elevations were observed in liver, adrenal gland, and lung concentrations (in descending order). Norfluoxetine concentrations far exceeded fluoxetine concentrations in tissues. As in the plasma, this was detected 2 months after termination of fluoxetine administration, such levels were approximately 1% at the time of treatment termination.

In cats, it has been used to avoid marking (urine) with good results after 8 weeks of age.

CONTRAINDICATIONS:
Do not use it in animals with hypersensitivity to it. Do not use in cats that are being medicated with "selegiline" due to a potentially lethal interaction.

GENERAL PRECAUTIONS:
Beagle dogs have tolerated single oral doses of 100 mg/kg of fluoxetine, presenting some adverse effects such as mydriasis and vomiting.

WARNINGS:
To minimize the risk of adverse reactions, the recommended dose should not be exceeded.
The most common reactions are decreased appetite, lethargy, and irregular urination, but there may be: vomiting, sedation, mydriasis, nausea, and gastrointestinal disorders. Phospholipidosis was identified as a major toxicological effect of fluoxetine after chronic administration in dogs and was observed in the lungs, liver, adrenal glands, lymph nodes, spleen, and peripheral leukocytes in animals receiving the high dose. Although there were no cardiovascular effects, a slight decrease in basal heart rate was observed in dogs.

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USE IN: Domestic canines

ROUTE OF ADMINISTRATION: Oral.

Canine dose: 1-2 mg/kg body weight.

Domestic canines:10 mg tablets

SIZE	Kg of body weight	Number of tablets
Miniature	2 - 5	¼ to ½
Small	5 - 10	½ to 1
Medium	10 -15	1 to 1 1/2
Large	20 - 30 30 - 40	2 to 3 3 to 4
Giant	40 - 50	4 to 5

Every 24 hrs. The treatment is recommended for at least 4 weeks or more according to the clinical case and criteria of the Veterinary Doctor.

PRESENTATION:
Box with blister of 10 tablets of 10 mg

STORAGE RECOMMENDATIONS:
Store in a cool, dry place at no more than 25ºC (77ºF).

PROTECTION LEGENDS:
Protect yourself from light.
Consult the Veterinarian Doctor.
Keep out of reach of children.
Its sale requires a quantified medical prescription.

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PRODUCT FOR EXCLUSIVE USE IN VETERINARY MEDICINE.
GLP-22

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