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# Selegiline (L-Deprenyl) Hydrochloride (Anipryl, Eldepryl, Carbex)

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(For veterinary information only)

WARNING

*The size of the tablet/medication is NOT an indication of a proper dose. Never administer any drug without your veterinarian's input. Serious side effects or death can occur if you use drugs on your pet without your veterinarian's advice.*

*It is our policy not to give dosing information over the Internet.*

## Brand Name: Anipryl, Eldepryl, Carbex

Available in 1.25 mg, 2 mg, 5 mg, 10 mg, 15 mg, 30 mg tablets, and 5 mg capsules

## Background

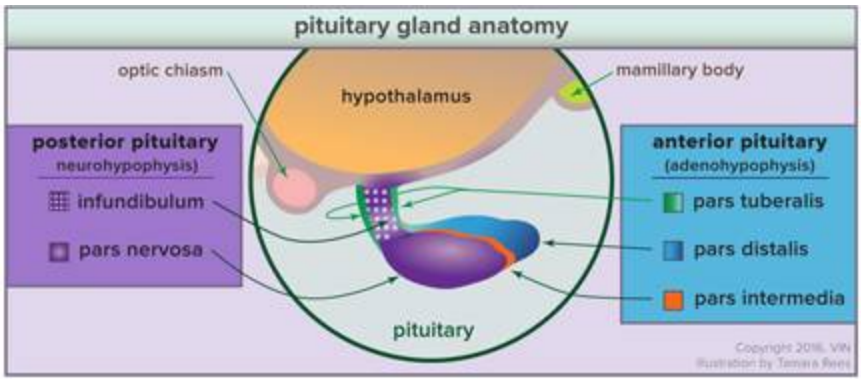
Selegiline Hydrochloride is, among other things, a monoamine oxidase inhibitor (also called an MAO inhibitor, a term that is a little more mainstream). In order to know what that means, we need to start with monoamine oxidase and why we might want to inhibit it. Monoamine oxidases are enzymes we have in two areas: the brain (monoamine oxidase inhibitor -B) and in the liver/GI tract (monoamine oxidase inhibitor -A). We will not be concerning ourselves with MAO-A as our interest lies in the brain.

In the brain, enzymes break down used neurotransmitters (chemicals that enable nerves to communicate). One of these neurotransmitters is called dopamine. Type B monoamine oxidases are responsible for getting rid of dopamine when it is no longer needed. Sometimes, however, it is beneficial to have dopamine stick around a bit and this is why we might want to inhibit monoamine oxidase B.

Selegiline Hydrochloride in the body is converted into three products: two stimulants and a type B monoamine oxidase inhibitor (an MAO-B inhibitor). These three products all produce the effects of Selegiline Hydrochloride.

There are two approved indications for Selegiline Hydrochloride in dogs: treating pituitary-dependent Cushing's disease, an excess in corticosteroid hormone production stemming from a pituitary tumor, and treating senile mental deterioration (canine cognitive dysfunction). The use of Selegiline Hydrochloride in dogs with Cushing's disease has met with limited success despite its FDA approval for this use. Since trilostane and lysodren are virtually the only medications used for Cushing's disease, you may wish to skip to the Cognitive Dysfunction section.

## Cushing's Disease




Cushing's disease is the insidious debilitating hormone imbalance that results when the adrenal glands overproduce cortisone. Most cases (85%) occur as the result of a tumor in the pituitary gland that produces a stimulatory hormone called ACTH. This hormone leads both adrenal glands to enlarge and overproduce cortisone, which in turn leads to symptoms associated with Cushing's disease.

Treatment has traditionally centered on suppressing adrenal gland production and release of cortisone but this approach has been fraught with potential for side effects. Selegiline Hydrochloride has allowed for a new approach by suppressing the pituitary gland directly.

We have mentioned that an MAO-B inhibitor allows for more dopamine in the brain. One of the functions of dopamine is the regulation, specifically the inhibition, of ACTH.

By using a monoamine oxidase-B inhibitor, dopamine is not broken down; instead, it persists and provides extra inhibition of ACTH. Selegiline Hydrochloride further acts on the enzymes that produce dopamine so that more dopamine is produced.

Selegiline Hydrochloride is a monoamine oxidase inhibitor specific to the brain's monoamine oxidases; those of the liver/GI tract are not affected. This effect on ACTH inhibition allows for the treatment of pituitary-dependent Cushing's disease in dogs as well as the treatment of Parkinson's syndrome in humans.

There is an important caveat in the use of Selegiline Hydrochloride for treating Cushing's disease. While 85 percent of dogs with Cushing's disease have pituitary tumors, only about 20 percent of them have tumors in the pars intermedia of the pituitary gland, which is where ACTH is dependent on dopamine. This means that if a dog with pituitary Cushing's disease is not one of these 20 percent, the only effect Selegiline Hydrochloride will have will be a general stimulatory effect from its metabolites (see below).

### Cognitive Dysfunction

Pet owners have long been frustrated by age-related behavior problems involving loss of house training, apparent memory loss or disorientation, sleep disturbances (either waking at the wrong time or sleeping unusually deeply), and loss of interest in social activities with the family. Such behavior changes are often written off as normal aging. One study at the University of California Davis School of Veterinary Medicine demonstrates how common these observations are: out of 69 dogs participating, 32 percent of 11-year-old dogs were affected by this syndrome, and 100 percent of dogs 16 years of age older were affected.

Still, the high frequency with which the syndrome is seen in older dogs does not make it normal. Other studies have shown that dogs affected by this syndrome show deposition of a protein called amyloid in their brains in patterns similar to the amyloid plaques found in the brains of humans with Alzheimer's disease.

Cognitive dysfunction is associated with the depletion of dopamine, the neurotransmitter mentioned above. As described above, Selegiline Hydrochloride also helps prolong dopamine activity, which may account for part of its efficacy in treating cognitive dysfunction. Further, dopamine breakdown results in harmful biochemicals known as free radicals. The stimulating metabolites are also helpful in improving the activity of senior patients, though, these same metabolites can also be responsible for adverse reactions as described below. The use of Selegiline Hydrochloride also helps reduce amounts of free radicals in the brain. The stimulating metabolites are also helpful in improving the activity of senior patients, though, these same metabolites can also be responsible for adverse reactions as described below.

### How this Medication is Used

Selegiline Hydrochloride is given once a day for two months. If no response is seen in this time, the dose is doubled for an additional month. If still no response is seen, another form of treatment should be pursued. Of the 69 dogs with cognitive dysfunction mentioned above, approximately 76 percent showed improvement on Selegiline Hydrochloride after one month of therapy. Some dogs improve in the first few days or weeks, some dogs do not show improvement until the second month. Often dogs would continue to improve during the first three months.

Selegiline Hydrochloride is given once daily, with or without food. If a dose is accidentally skipped, the next dose should be given as scheduled. Do not double up on medication doses.

### Side Effects

There is a 5 percent incidence of unacceptable side effects with Selegiline Hydrochloride treatment. These side effects include: vomiting, diarrhea, appetite loss, itchy skin, tremors, drooling, listlessness, disorientation, diminished hearing, or restlessness.

When three times the recommended dose was used in dogs, salivation, weight loss, panting, dehydration, pacing, and poor pupil response to light were observed. Obviously, these signs should not be observed with the normal use of the medication.

It should be noted that after oral administration, Selegiline Hydrochloride is processed by the liver to produce amphetamine and methamphetamine, both of which are stimulants. Humans that take Selegiline Hydrochloride have reported assorted behavioral side effects so it is important to watch for undesirable changes that might be resulting from the medication.

### Interactions with other Drugs

Serotonin syndrome is a potential side effect that can occur if brain levels of serotonin get too high. Elevated heart rate, tremors/shivering, dilated pupils, difficulty breathing, elevated body temperature, or high blood pressure can all be signs of serotonin syndrome. Animals with serotonin syndrome sometimes demonstrate general hyperactivity as a sign that something is wrong. Death can result if blood pressure rises too high. Because of this syndrome, medications that elevate serotonin levels should not be combined. The following interactions are avoided to prevent the possibility of serotonin syndrome

- Selegiline Hydrochloride has been used in conjunction with alprazolam and propranolol for phobias.

- MAO inhibitors should not be combined as MAO inhibitors all act by increasing serotonin levels. This is generally not an issue in veterinary medicine with one exception: amitraz. Amitraz has become a popular acaricide (killer of ticks and

mites) and has been incorporated into many flea and tick products.

- Selegiline Hydrochloride should not be used with fluoxetine. Because of fluoxetine's ability to last a long time in the body, a 5-week period is recommended between the discontinuing fluoxetine and the initiation of Selegiline Hydrochloride. Other psychoactive drugs not compatible with MAO-B inhibitors include mirtazapine, amitriptyline, and clomipramine.

- Selegiline Hydrochloride should not be used with phenylpropanolamine, a common medication used to manage urinary incontinence in older dogs. If your dog is already on phenylpropanolamine and you wish to try Selegiline Hydrochloride, it is important to have discontinued phenylpropanolamine for at least two weeks before beginning Selegiline Hydrochloride. High blood pressure can result from the use of these two medications together.

- In humans, dangerous drug interactions have occurred when Selegiline Hydrochloride has been combined with meperidine (Demerol®). It is unclear how dangerous other narcotics might be so it is recommended that no narcotic be combined with Selegiline Hydrochloride, especially not meperidine. This caveat includes concurrent use with tramadol as well even though tramadol is not metabolized into a narcotic in dogs.
- Probably the most serious adverse reaction/drug interaction that could occur with Selegiline Hydrochloride is serotonin syndrome. This potential side effect can occur if brain levels of serotonin get too high.
- Other medications that could increase the risk of serotonin syndrome are metoclopramide, commonly used for nausea, and trazodone, a tranquilizer.

Learn more about canine cognitive dysfunction and the use of Anipryl.

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