Mirtazapine

BRAND NAME: MIRATAZ, REMERON

AVAILABLE IN
7.5 mg, 15 mg, 30 mg, 45 mg
TABLETS
AND A TRANSDERMAL GEL APPROVED
FOR CATS

BACKGROUND

Mirtazapine was developed for human use as an antidepressant for moderate to severe depression. It is not a tricyclic antidepressant like clomipramine or amitriptyline but is actually a member of the “tetracyclic” class, because it has four chemical rings, rather than three, in its structure. Mirtazapine acts to increase norepinephrine and serotonin in the brain, though there is some question as to how this is actually accomplished. Norepinephrine is a stimulating neurotransmitter and serotonin is a neurotransmitter associated with relaxation and comfort, thus increasing the brain levels of these substances could be very helpful in treating depression.

While there is certainly a call for anti-anxiety pharmaceuticals in veterinary medicine, it is generally its side effects which make mirtazapine such a desirable medication for animals. Mirtazapine is mostly used for its appetite stimulating side effects to support animals when appetite is poor. Mirtazapine also exerts anti-nausea effects by acting on the neurorecpetors in the intestine and stomach which in turn communicate with the vomit center of the brain. Obviously, a medication that addresses both nausea and appetite loss is a boon to treating many medical conditions. Apparently mirtazapine increases central nervous system serotonin but counteracts serotonin-activity in the gastrointestinal tract, which is how it exerts the effects that we like.

Mirtazapine comes in a regular formula as well as a rapid-dissolving formula. Either may be used in animals. Recently, a special feline formula has been introduced. This formula is a transdermal gel which is applied to the inner surface of the ear and is absorbed directly through the skin as described below.

HOW THIS MEDICATION IS USED

Mirtazapine is used in the treatment of conditions where poor appetite and nausea go together such as in the treatment of intestinal/stomach disease, liver or kidney disease, or any other condition involving both nausea and appetite loss. Mirtazapine can also be used to alleviate the nausea/appetite loss that accompanies the treatment of cancer by chemotherapy.

Oral Use in Dogs
In dogs, mirtazapine is generally given in tablet form once daily. Newer studies suggest this may not be frequent enough but an alternative protocol has not been devised. If mirtazapine does not seem effective for a dog, consider a different product such as capromorelin or cyproheptadine.

Oral Use in Cats
The tablet form can also be used in cats but is given every 1, 2 or 3 days. The problem with oral use in the cat is that the human 15mg tablet cannot easily be cut smaller than into quarters. While this size dose certainly works for appetite improvement in cats, more side effects are seen with this dose. Mirtazapine works best when a smaller dose is used daily rather than when a larger dose is used less frequently. On the flip side of this, however, is the reputation of many cats for being difficult with regard to oral medication. Pilling 2-3 times per week may end up being more practical than getting a compounded medication in a smaller strength for daily dosing.

Transdermal Use in Cats
The new transdermal gel form for cats is applied to the skin of the inner ear once daily. Gloves are required and the product includes a ruler so as to measure a stripe of the appropriate dose on the gloved finger. This amount is then rubbed on the cat's ear skin. Contact with the cat should be avoided for 2 hours after the product is applied so that it may absorb through the skin undisturbed. The human should dispose of the gloves and wash their hands after the application is complete. Although the product is used daily, the ear receiving the application should be alternated daily (right ear one day, left ear the next, for example).

Cats with Liver Disease
In the event of liver disease or kidney disease, the clearance of this drug from the body is reduced by approximately 30% so ideally the dosing interval should also be reduced. Check with your veterinarian for instructions.

Mirtazapine also has antihistamine properties but it is unlikely to be used for these when so many other antihistamines are more readily available.

SIDE EFFECTS

The most common reported side effect of this medication is drowsiness, though hyperactivity was reported in 11% of cats using the transdermal gel. In cats, increased affectionate behavior is reported as well as increased vocalization.

Mirtazapine decreases cortisol secretion by the adrenal glands but has not actually panned out as a treatment for Cushing's Syndrome, where excess adrenal steroids are produced by the adrenal glands.

Serotonin syndrome is a potential side effect should brain levels of serotonin get too high but this syndrome generally requires a combination of serotonin-increasing medications. 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. If there is any question that serotonin syndrome is occurring, cyproheptadine can be used as an antidote.

At higher doses, mirtazapine may cause a drop in blood pressure or an elevation in heart rate.

Occasionally, mirtazapine has been reported to cause abnormalities in blood cell lines developing in the bone marrow. If a patient is known to have leukemia, low platelets, or some other blood disease mirtazapine can still be used but extra monitoring tests are probably in order.

INTERACTIONS WITH OTHER DRUGS

Inhibitors of Monoamine Oxidase-A cannot be used with miratazpine, as this combination increases the risk of the aforementioned serotonin syndrome. Fortunately, MAO-A inhibitors are not used in veterinary medicine so this is of little concern (The exception would be amitraz, the active ingredient in several canine anti-tick products as well as in Mitaban® dip used against mange mites in dogs. Amitraz is both an MAO-A and MAO-B inhibitor). The only other MAO inhibitor used in veterinary medicine is selegiline which is an MAO-B inhibitor and a 14 day "wash out" period is recommended between the use of selegiline and mirtazapine.

Use of mirtazapine with selective serotonin reuptake inhibitors ("SSRI's")can raise brain serotonin levels high enough to create "serotonin syndrome" as mentioned above. Mirtazapine should not be used with these drugs. The most commonly used SSRI in veterinary medicine would be fluoxetine. Other medications that increase the risk of serotonin syndrome when used concurrently with mirtazapine include: tramadol (pain reliever), buspirone (anti-anxiety medication), cimetidine (antacid), erythromycin (antibiotic), ketoconazole (antifungal), metoclopramide (stomach motililty modifier), and narcoticpain relievers.

CONCERNS AND CAUTIONS

Safety of mirtazapine is unproven in pregnancy and lactation.

Patients with liver or kidney disease should receive a reduced dose of mirtazapine or a reduction in the dosing schedule as discussed above.

The feline transdermal gel product has not been tested in cats under 2 kg (4.4 lbs) in body weight nor in cats under 6 months of age.

Mirtazapine use can increase liver enzyme test values. These elevations disappear within one month of drug withdrawal.

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