Introducing Mirataz™ (mirtazapine transdermal ointment)

The first and only FDA-approved transdermal medication for the management of weight loss in cats

“ANOTHER PILL? GIVE IT TO THE DOG.”

Important Safety Information

Mirataz™ (mirtazapine transdermal ointment) is for topical use in cats only under veterinary supervision. Do not use in cats with a known hypersensitivity to mirtazapine or any of the excipients. Do not use in cats treated with monoamine oxidase inhibitors (MAOIs). Not for human use. Keep out of reach of children. Wear gloves when handling/applying, wash hands after and avoid contact between the treated cat and people or other animals for 2 hours following application. Use with caution in cats with hepatic and kidney disease. Cat’s food intake should be monitored upon discontinuation. Safety has not been evaluated in cats less than 2 kg, less than six months of age or in breeding, pregnant or lactating cats. The most common adverse reactions observed during clinical trials were application site reactions, behavioral abnormalities (vocalization and hyperactivity) and vomiting. For product label, including complete safety information, see pages 10-11.
Identify and manage unintended weight loss in cats

Weight loss is a clinical sign associated with various underlying diseases in the cat

Asking the right questions can make the difference for the cats in your practice. While there are often subtle changes that the cat owner may or may not have noticed, early detection and action allows the cat to begin eating again, while you diagnose the underlying condition.

**QUESTIONS TO ASK YOUR CLIENTS**

- “Tell me how your cat behaves when he or she eats.”
- “How would you describe your cat’s appetite?”
- “Describe your cat’s eating behavior.”
- “How many times does your cat visit the food bowl?”
- “Describe your typical feeding routine with your cat.”
- “Tell me how your cat’s eating habits have changed.”

Prolonged inadequate nutrition may be more detrimental to the patient than the primary disease process

Therefore, both identifying weight loss and diagnosing the underlying cause are important. Once changes in eating behavior, body weight, and body condition have been identified and discussed with the cat owner, the tailored diagnostic investigation is initiated, guided by a thorough history and physical exam.

Some of the more common underlying diseases could be:

- Hyperthyroidism
- Chronic kidney disease
- Inflammatory bowel disease
- Neoplasia
- Pancreatitis
- Liver failure

Important Safety Information

Mirataz™ (mirtazapine transdermal ointment) is for topical use in cats only under veterinary supervision. Do not use in cats with a known hypersensitivity to mirtazapine or any of the excipients or in cats treated with monoamine oxidase inhibitors (MAOIs). Not for human use. Keep out of reach of children. Wear gloves to apply and wash hands after. Avoid contact with treated cat for 2 hours following application. The most common adverse reactions include application site reactions, behavioral abnormalities (vocalization and hyperactivity) and vomiting. For product label, including complete safety information, see pages 10-11.

Mirataz™ (mirtazapine transdermal ointment) manages weight loss in cats

A survey of US veterinarians indicates that ~9,000,000 cats present with weight loss/inappetence due to underlying conditions

Only 2 million of those cats are prescribed medication (compounded or human generic mirtazapine) to manage their weight loss

74% of veterinarians indicated that the ease of administering a medication is one of the most important factors in selecting a medication for the management of weight loss in cats

With Mirataz, veterinarians can confidently recommend an effective topically applied product for cats with unintended weight loss that may be associated with underlying disease

- Mirataz is the first and only FDA-approved transdermal medication for the management of weight loss in cats
- In clinical studies, Mirataz resulted in significant weight gain in cats in as little as 14 days following topical application of 2 mg per day
- Mirataz gives your clients a practical way to manage their cat’s weight loss without administration of oral medication and does not rely on the cat to eat to be medicated
- Due to proprietary Accusorb™ technology, Mirataz achieves measurable plasma concentrations of mirtazapine in cats
- Mirataz was well tolerated both locally and systemically in clinical studies

About Mirataz

~9,000,000 cats present with weight loss/inappetence due to underlying conditions

Only 2 million of those cats are prescribed medication (compounded or human generic mirtazapine) to manage their weight loss

74% of veterinarians indicated that the ease of administering a medication is one of the most important factors in selecting a medication for the management of weight loss in cats

With Mirataz, veterinarians can confidently recommend an effective topically applied product for cats with unintended weight loss that may be associated with underlying disease

- Mirataz is the first and only FDA-approved transdermal medication for the management of weight loss in cats
- In clinical studies, Mirataz resulted in significant weight gain in cats in as little as 14 days following topical application of 2 mg per day
- Mirataz gives your clients a practical way to manage their cat’s weight loss without administration of oral medication and does not rely on the cat to eat to be medicated
- Due to proprietary Accusorb™ technology, Mirataz achieves measurable plasma concentrations of mirtazapine in cats
- Mirataz was well tolerated both locally and systemically in clinical studies

For product label, including complete safety information, see pages 10-11.
Mirataz™ (mirtazapine transdermal ointment): the first and only FDA-approved transdermal medication for cats

The active ingredient in Mirataz is mirtazapine

The pharmacodynamic action of mirtazapine involves antagonism of several receptor sites

- Antagonism of presynaptic α-2 receptors, serotonin receptors (5-HT2A, 5-HT2C, 5-HT3), and histamine receptors (H1) by mirtazapine has been demonstrated to result in:
  - Appetite stimulation via interaction with nuclei within the hypothalamus
  - Enhanced release of both serotonin (5-HT) and noradrenaline (NE)
  - Reduced nausea and vomiting in cats

*Vomiting was reported in clinical field studies with the use of Mirataz.

A single dose (0.5 mg/kg) of mirtazapine transdermal ointment applied topically produced a mean plasma Cmax (21.5 ng/mL) approximately one-fourth the mean Cmax seen with a single dose of mirtazapine transdermal ointment administered orally (83.1 ng/mL). Cmax may be related to adverse effects.

While not FDA approved, human and compounded versions of mirtazapine have been used off-label but may not be ideal for every cat

- Human tablets must be split or broken, which results in inaccurate dosing
- Oral products placed on food will work only if the cat is eating
- Liquids by mouth may not be any easier than pilling
- Compounded transdermal mirtazapine has been shown to result in inconsistent and highly variable blood mirtazapine levels

Important Safety Information

Mirataz™ (mirtazapine transdermal ointment) is for topical use in cats only under veterinary supervision. Do not use in cats with a known hypersensitivity to mirtazapine or any of the excipients or in cats treated with monoamine oxidase inhibitors (MAOIs). Not for human use. Keep out of reach of children. Wear gloves to apply and wash hands after. Avoid contact with treated cat for 2 hours following application. The most common adverse reactions include application site reactions, behavioral abnormalities (vocalization and hyperactivity) and vomiting. For product label, including complete safety information, see pages 10-11.

Mirataz achieves measurable blood levels of mirtazapine and effectively results in weight gain in cats

Mirataz demonstrated a 3.9% increase in body weight in cats with unintended weight loss in as little as 14 days.

Study Design: Randomized, double-blind, placebo-controlled study (N=177)
The safety profile of Mirataz™
(mirtazapine transdermal ointment)

230 cats were enrolled in a field study to assess the clinical safety and effectiveness of Mirataz. Cats enrolled in the study with underlying disease may have received concurrent medications.6

CONCOMITANT MEDICATIONS ADMINISTERED
[OCCURRING IN >3% OF CATS IN ANY TREATMENT GROUP [EFFECTIVENESS POPULATION]]6

<table>
<thead>
<tr>
<th>Concomitant Medication Category</th>
<th>Mirataz [n=52/83 (%)]</th>
<th>Placebo [n=67/94 (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic</td>
<td>11 (13.3%)</td>
<td>17 (18.1%)</td>
</tr>
<tr>
<td>Vitamin/mineral</td>
<td>9 (10.8%)</td>
<td>16 (17.0%)</td>
</tr>
<tr>
<td>Parenteral fluids</td>
<td>8 (9.6%)</td>
<td>10 (10.6%)</td>
</tr>
<tr>
<td>Anti-thyroid drug</td>
<td>8 (9.6%)</td>
<td>6 (6.4%)</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>8 (9.6%)</td>
<td>5 (5.3%)</td>
</tr>
<tr>
<td>Vaccine</td>
<td>6 (7.2%)</td>
<td>8 (8.5%)</td>
</tr>
<tr>
<td>Anti-hypertensive</td>
<td>5 (6.0%)</td>
<td>5 (5.3%)</td>
</tr>
<tr>
<td>Supplement</td>
<td>4 (4.8%)</td>
<td>14 (14.9%)</td>
</tr>
<tr>
<td>Anthelminic or antiparasitic</td>
<td>4 (4.8%)</td>
<td>9 (9.6%)</td>
</tr>
<tr>
<td>Antacid</td>
<td>4 (4.8%)</td>
<td>3 (3.2%)</td>
</tr>
<tr>
<td>Opioid</td>
<td>3 (3.6%)</td>
<td>8 (8.5%)</td>
</tr>
<tr>
<td>Laxative</td>
<td>3 (3.6%)</td>
<td>3 (3.6%)</td>
</tr>
<tr>
<td>Otic</td>
<td>3 (3.6%)</td>
<td>1 (1.1%)</td>
</tr>
</tbody>
</table>

The most common adverse reactions observed in the clinical field study included application-site reactions, vocalization, hyperactivity, and vomiting.8

► Application-site reactions resolved upon discontinuation of dosing8
► Of the Mirataz-treated cats that experienced vomiting, 26% had vomiting at the time of enrollment due to underlying conditions8

ADVERSE REACTIONS REPORTED DURING THE CLINICAL FIELD STUDY
[OCCURRING IN >3% OF CATS IN THE MIRATAZ GROUP [SAFETY POPULATION]]8

<table>
<thead>
<tr>
<th>Description of Adverse Reaction</th>
<th>Mirataz [n=115 (%)]</th>
<th>Placebo [n=115 (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Site (ear pinna)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythema</td>
<td>12 (10.4%)</td>
<td>20 (17.4%)</td>
</tr>
<tr>
<td>Behavioral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vocalization (including crying, mewing)</td>
<td>13 (11.3%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Hyperactivity (including pacing, restlessness, sleeplessness)</td>
<td>8 (7.0%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Disoriented state or ataxia</td>
<td>4 (3.5%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Lethargy (including depressed, sedation, or weakness)</td>
<td>4 (3.5%)</td>
<td>9 (7.8%)</td>
</tr>
<tr>
<td>Physical Examination or Observational</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>13 (11.3%)</td>
<td>15 (13.0%)</td>
</tr>
<tr>
<td>Dehydration</td>
<td>6 (5.2%)</td>
<td>5 (4.3%)</td>
</tr>
<tr>
<td>Diarrhea or soft stool</td>
<td>6 (5.2%)</td>
<td>7 (6.1%)</td>
</tr>
<tr>
<td>Heart murmur</td>
<td>5 (4.3%)</td>
<td>7 (6.1%)</td>
</tr>
<tr>
<td>Inappetence</td>
<td>5 (4.3%)</td>
<td>5 (4.3%)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>4 (3.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Clinical Pathology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>7 (6.1%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Elevated BUN (without creatinine)</td>
<td>6 (5.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Elevated creatinine and BUN</td>
<td>5 (4.3%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
<td>5 (4.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>5 (4.3%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Pyuria</td>
<td>5 (4.3%)</td>
<td>0</td>
</tr>
</tbody>
</table>

► Elevated BUN levels were not considered clinically relevant and were likely due to the increased incidence of renal disease (based on clinical pathology and urinalysis) at the time of enrollment in the Mirataz group8
Pets bring a great amount of joy to our lives

In fact, 66% of pet owners believe their pet helps lower stress.\(^\text{1,2}\)

If their cat is experiencing unintended weight loss associated with various underlying conditions, that news alone can be worrisome.

Ensuring at-home treatment plans addressing both the medical needs of the cat and protecting the human-animal bond can be challenging.

With Mirataz\(^\text{TM}\) (mirtazapine transdermal ointment), you can confidently recommend an effective topically applied product for cats with unintended weight loss that may be associated with underlying disease.

Dosing and administration

Administer topically by applying a 1.5-inch ribbon of ointment (approximately 2 mg/cat) on the inner pinna of the cat’s ear once daily for 14 days (see diagrams below)

1. Step 1: Wear disposable gloves. Twist cap on tube counterclockwise to open.

2. Step 2: Apply even pressure on tube and squeeze a 1.5-inch line of ointment onto your gloved finger using the measured line on the carton or in the package insert.

3. Step 3: Using your gloved finger, gently rub ribbon of ointment on inside pinna of the cat’s ear spreading it evenly over the surface. Dispose of used gloves after each application. If contact with your skin occurs wash thoroughly with soap and warm water.

Important Safety Information

Mirataz\(^\text{TM}\) (mirtazapine transdermal ointment) is for topical use in cats only under veterinary supervision. Do not use in cats with a known hypersensitivity to mirtazapine or any of the excipients or in cats treated with monoamine oxidase inhibitors (MAOIs). Not for human use. Keep out of reach of children. Wear gloves to apply and wash hands after. Avoid contact with treated cat for 2 hours following application. The most common adverse reactions include application site reactions, behavioral abnormalities (vocalization and hyperactivity) and vomiting. For product label, including complete safety information, see pages 10-11.
Mirtaz™ (mirtazapine transdermal ointment)

**INDICATIONS:** Mirtaz™ is indicated for the management of weight loss in cats.

**DOSAGE AND ADMINISTRATION:**

- Administration topically using a 1.1 inch rod of ointment (approximately 2 mg/cat) on the inner pinna of the ear once daily for 14 days (less Diagrams below).

- Wear disposable gloves when applying Mirtaz™. Dispose of used gloves after each application. If solutions with your skin soak, wash thoroughly with soap and water.

**CONTRAINDICATIONS:**

- Mirtaz™ is contraindicated in cats with a known hypersensitivity to mirtazapine or any of the ingredients.

- Mirtaz™ should not be given in combination, or within 14 days before or after treatment with a monoamine oxidase inhibitor (MAOI) [e.g. selegiline hydrochloride (L-deprenyl), amitraz], as there should be careful consideration as to the combination of antidepressants considered.  

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cmax</td>
<td>μg/mL</td>
<td>419.3 (213)</td>
</tr>
<tr>
<td>AUC</td>
<td>h*μg/mL</td>
<td>112.2 (28)</td>
</tr>
</tbody>
</table>

- Effective plasma concentrations at steady state after 1mg dose of mirtazapine topically at the inner pinna of the ear

- The effectiveness of Mirtaz™ (mirtazapine transdermal ointment) was demonstrated in a 12-week, placebo-controlled, multi-site study involving client-owned cats of various breeds and ages.

**PRECAUTIONS:**

- Do not administer orally or to the eye.

- Use caution in cats with hepatic disease. Mirtazapine may cause increased serum liver enzymes (See Adverse Reactions).

- Use caution in cats with chronic kidney disease. kidney disease may cause increased serum liver enzymes which may result in higher drug exposure.

- Upon discontinuation of Mirtaz™, it is important to monitor the cat’s food intake. Food intake should be reduced to maintain the weight gain that has been achieved with Mirtaz™.

- If food intake is depressed to less than 80% of pre-treatment levels, reduce the dose or discontinue as needed.

- Mirtaz™ has not been evaluated in cats 2 kg or less or in cats of age 6 months or younger.

- Use caution in pregnant, lactating, or breeding cats. In a 6-week laboratory safety study, 48 healthy cats aged 7-10 months were dosed topically with Mirtaz™. The cats were 2.8-24.6 years of age.

- Mirtaz™ should not be given in combination, or within 14 days before or after treatment with a monoamine oxidase inhibitor (MAOI) [e.g. selegiline hydrochloride (L-deprenyl), amitraz].

- If other drugs or combinations are to be administered concurrently, the clinician should be aware of the individual drug's pharmacology and potential to influence the effects of mirtazapine.

**ADVERSE REACTIONS:**

- In a randomized, double-blind, vehicle-controlled field study to assess the effectiveness and safety of mirtazapine for the management of weight loss in cats, 115 cats treated with Mirtaz™ and 115 cats treated with vehicle control were evaluated for safety. The vehicle control was an inert component containing the same excipients as Mirtazapine ointment. The most common adverse reaction included application site reactions, behavioral abnormalities (excitation and hyperactivity), and vomiting. The most common adverse reactions and their frequency (daily incidence and number of cats) are presented in Table 1.

**INFORMATION FOR CAT OWNERS:**

- Upon discontinuation of Mirtaz™, it is important to monitor your cat’s food intake. Your cat’s food intake should be reduced to maintain the weight gain achieved with Mirtaz™.

**CLINICAL PHARMACOLOGY:**

**Molecular Formula:** C17H19N3

**Molecular Weight:** 265.35

**Physical Examination or Observational Parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight</td>
<td>g</td>
<td>3.71 (1.6)</td>
</tr>
<tr>
<td>Body length</td>
<td>cm</td>
<td>18.9 (1.6)</td>
</tr>
<tr>
<td>Tail length</td>
<td>cm</td>
<td>8.9 (1.6)</td>
</tr>
<tr>
<td>Ears</td>
<td>cm</td>
<td>2.9 (1.6)</td>
</tr>
<tr>
<td>Heart rate</td>
<td>/min</td>
<td>144 (24)</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>/min</td>
<td>28 (4)</td>
</tr>
<tr>
<td>Temperature</td>
<td>°C</td>
<td>37.8 (0.2)</td>
</tr>
</tbody>
</table>

- The effectiveness of Mirtaz™ (mirtazapine transdermal ointment) was demonstrated in a 12-week, placebo-controlled, multi-site study involving client-owned cats of various breeds.

**PRINCIPAL PHARMACOLOGICAL ACTIONS:**

- Mirtaz™ is a potent antagonist at serotonergic 5-HT2A receptors, which may account for the observed increase in weight gain. Mirtaz™ is also a potent antagonist at histaminergic H1 receptors, which may account for the observed increase in weight gain.

**ELEVATED BUN (without creatinine)**

- Elevated BUN (without creatinine) was observed in 4 cats in the Mirtaz™ group. Elevated creatinine was not observed in any cats in either group.

**DISPOSITION:**

After discontinuation of Mirtaz™, it is important to monitor your cat’s food intake. Your cat’s food intake should be reduced to maintain the weight gain achieved with Mirtaz™. The most common adverse reactions and their frequency (daily incidence and number of cats) are presented in Table 1.

**ANTIPSYCHOTIC-INDUCED WEIGHT LOSS:**

- Antipsychotic-induced weight loss is believed to be due to inhibition of brain monoamine neurons (e.g., norepinephrine, dopamine, serotonin), which results in decreased appetite and food intake.

**SUMMARY:**

Mirtaz™ (mirtazapine transdermal ointment) is a white to off-white ointment containing 2% (w/w) mirtazapine transdermal ointment. The structural formula of mirtazapine is: C_{17}H_{19}N_{3} O. Molecular Formula: C_{17}H_{19}N_{3} Molecular Weight: 265.35

**Mirtazapine**

**References:**


3. Burlingame, CA 94010


5. Efforts to lower weight in women with obesity. The New England Journal of Medicine, 357(2), 160-168.


Manage weight loss in cats with Mirataz™ (mirtazapine transdermal ointment)

✔ Mirataz is the first and only FDA-approved transdermal medication for the management of weight loss in cats

✔ In clinical studies, Mirataz resulted in significant weight gain in cats in as little as 14 days following topical application of 2 mg per day.

✔ Mirataz gives your clients a practical way to manage their cat’s weight loss without administration of oral medication and does not rely on the cat to eat to be medicated

✔ Due to proprietary Accusorb™ technology, Mirataz achieves measurable plasma concentrations of mirtazapine in cats.

✔ Mirataz was well tolerated both locally and systemically in clinical studies.

“ANOTHER PILL? GIVE IT TO THE DOG.”

Important Safety Information

Mirataz™ (mirtazapine transdermal ointment) is for topical use in cats only under veterinary supervision. Do not use in cats with a known hypersensitivity to mirtazapine or any of the excipients. Do not use in cats treated with monoamine oxidase inhibitors (MAOIs). Not for human use. Keep out of reach of children. Wear gloves when handling/applying, wash hands after and avoid contact between the treated cat and people or other animals for 2 hours following application. Use with caution in cats with hepatic and kidney disease. Cat’s food intake should be monitored upon discontinuation. Safety has not been evaluated in cats less than 2 kg, less than six months of age or in breeding, pregnant or lactating cats. The most common adverse reactions observed during clinical trials were application site reactions, behavioral abnormalities (vocalization and hyperactivity) and vomiting. For product label, including complete safety information, see pages 10-11.


KindredBio

Mirataz™ and Accusorb™ are trademarks of KindredBio
©2018 Kindred Biosciences, Inc., Burlingame, CA 94010. All rights reserved
US-MAZ-1800011 May-15-2018