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"ANOTHER PILL? GIVE IT TO THE DOG."
Identifying causes of feline weight loss

Feline weight loss is often associated with underlying conditions

Some of the more common underlying diseases could be¹:  
- Hyperthyroidism 
- Chronic kidney disease 
- Inflammatory bowel disease 
- Neoplasia 
- Pancreatitis 
- Liver failure

Weight loss can also be linked to non-disease-related stressors

Changes in environment, stress from travel or medical procedures, or even changes in food can all cause variations in a cat’s eating habits.

Prolonged inadequate nutrition may be more detrimental to the patient than the primary disease process⁶

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.

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Mirataz® (mirtazapine transdermal ointment)

With Mirataz, veterinarians can confidently recommend an effective topically applied product for cats with unintended weight loss

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

- Human tablets must be split or broken, which may result in:  
  - Inaccurate dosing, which has been shown to result in accidental overdose and toxicity⁷  
  - Unknown user safety to humans handling cut or broken pills  
  - Unknown drug distribution in pill fragments  
- Oral products placed on food will work only if the cat is eating and fed individually  
- 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 levels⁸

Mirataz gives your clients an option for one less oral medication for their cats
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The first FDA-approved transdermal medication available for cats

The active ingredient in Mirataz is mirtazapine

Mirataz is classified pharmacologically as a weight gain drug

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:

- Orexigenic effect via interaction with nuclei within the hypothalamus
- Enhanced release of both serotonin (5-HT) and noradrenaline (NE)

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

Effectiveness of Mirataz® (mirtazapine transdermal ointment)

The off-label use of human mirtazapine tablets given orally to cats is based on extrapolation with no species-specific PK to support dosing

Mirataz, the FDA-approved mirtazapine transdermal ointment, has a similar elimination half-life to oral mirtazapine, but a lower Cmax, lower AUC, and longer Tmax

Pharmacokinetic data in the cats supports daily dosing. In cats with kidney or liver disease, it is desirable to limit peak serum concentrations and AUC to minimize drug exposure where metabolism and elimination or clearance may be impacted by organ function while still maintaining clinical effect.

MIRATAZ CONCENTRATIONS IN CATS AT STEADY STATE FOLLOWING DAILY DOsing (DAY 13; 0.5 MG/KG)
Mirataz® (mirtazapine transdermal ointment) safety profile

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.9

PRE-EXISTING CONDITIONS AND RELEVANT MEDICAL HISTORY OF CATS ENROLLED IN THE STUDY (SAFETY POPULATION)13

<table>
<thead>
<tr>
<th>Pre-existing Condition</th>
<th>Mirataz N=115 n (%)</th>
<th>Placebo N=115 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal</td>
<td>64 (55.7%)</td>
<td>48 (41.7%)</td>
</tr>
<tr>
<td>Multisystemic</td>
<td>56 (48.7%)</td>
<td>47 (40.9%)</td>
</tr>
<tr>
<td>Dental</td>
<td>35 (30.4%)</td>
<td>39 (33.9%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>31 (27.0%)</td>
<td>35 (30.4%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>25 (21.7%)</td>
<td>25 (21.7%)</td>
</tr>
<tr>
<td>Endocrine</td>
<td>24 (20.9%)</td>
<td>19 (16.9%)</td>
</tr>
<tr>
<td>Urinary</td>
<td>23 (20.0%)</td>
<td>32 (27.8%)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>22 (19.1%)</td>
<td>14 (12.2%)</td>
</tr>
<tr>
<td>Skin and aural</td>
<td>20 (17.4%)</td>
<td>15 (13.0%)</td>
</tr>
<tr>
<td>Behavioral</td>
<td>11 (9.6%)</td>
<td>16 (13.9%)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>8 (7.0%)</td>
<td>17 (14.8%)</td>
</tr>
<tr>
<td>Hepatobiliary</td>
<td>8 (7.0%)</td>
<td>4 (3.5%)</td>
</tr>
</tbody>
</table>

CONCOMITANT MEDICATIONS ADMINISTERED [OCCURRING IN >3% OF CATS IN ANY TREATMENT GROUP (SAFETY POPULATION)]14

<table>
<thead>
<tr>
<th>Concomitant Medication Category</th>
<th>Mirataz N=115 n (%)</th>
<th>Placebo N=115 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral fluids</td>
<td>20 (17.4%)</td>
<td>15 (13.0%)</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>19 (16.5%)</td>
<td>24 (20.9%)</td>
</tr>
<tr>
<td>Vitamin/Mineral</td>
<td>18 (15.7%)</td>
<td>18 (15.7%)</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>13 (11.3%)</td>
<td>7 (6.1%)</td>
</tr>
<tr>
<td>Anti-thyroid drug</td>
<td>12 (10.4%)</td>
<td>9 (7.8%)</td>
</tr>
<tr>
<td>Suplement</td>
<td>9 (7.8%)</td>
<td>16 (13.9%)</td>
</tr>
<tr>
<td>Anti-hypertensive</td>
<td>8 (7.0%)</td>
<td>9 (7.8%)</td>
</tr>
<tr>
<td>Vaccine</td>
<td>7 (6.1%)</td>
<td>10 (8.7%)</td>
</tr>
<tr>
<td>Opioid</td>
<td>6 (5.2%)</td>
<td>8 (7.0%)</td>
</tr>
<tr>
<td>Antacid</td>
<td>6 (5.2%)</td>
<td>6 (5.2%)</td>
</tr>
<tr>
<td>Antiemetic</td>
<td>6 (5.2%)</td>
<td>5 (4.3%)</td>
</tr>
<tr>
<td>Anthelmintic or Antiparasitic</td>
<td>5 (4.3%)</td>
<td>15 (13.0%)</td>
</tr>
<tr>
<td>Laxative</td>
<td>4 (3.5%)</td>
<td>5 (4.3%)</td>
</tr>
<tr>
<td>NSAID</td>
<td>4 (3.5%)</td>
<td>1 (0.9%)</td>
</tr>
</tbody>
</table>

The most common adverse events observed in the clinical field study included application-site reactions, vocalization, hyperactivity, and vomiting.17

- Of the Mirataz-treated cats that experienced vomiting, 27.8% had pre-existing vomiting at the time of enrollment due to underlying conditions.18

ADVERSE EVENTS REPORTED DURING THE CLINICAL FIELD STUDY [OCCURRING IN >3% OF CATS IN THE MIRATAZ GROUP (SAFETY POPULATION)]17

<table>
<thead>
<tr>
<th>Description of Adverse Event</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 group.17
Unintended weight loss can have significant consequences

Pets bring a great amount of joy to our lives

In fact, 66% of pet owners believe their pet helps lower stress.18

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.

Ideal body condition correlates to survival:

Analyzing patient records of more than 2,600 cats showed a body condition score (BCS) of 6 had the highest survival rate. Lifespan decreased when cats had a BCS less than 5 out of 9.20

This supports other research that shows being underweight puts cats at risk for damage to internal organs and increased susceptibility to infections.21

Helping clients identify the underlying causes of weight loss and maintaining their cat’s ideal body condition may help improve their pet’s lifespan and quality of life.

Dosing and administration

Administer topically by applying a 1.5-inch ribbon of ointment (approximately 2 mg/cat, equal to 0.1 mL) on the inner pinna of the cat’s ear once daily for 14 days (see diagrams below)

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

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.

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.

After application, care should be taken that people or other animals in the household do not come in contact with the treated cat for 2 hours because mirtazapine can be absorbed transdermally and orally.

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INFORMATION FOR CAT OWNERS:

To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact Kindled Bioscience, Inc. at 888-688-2548.

* One cat with renal insufficiency was reported with a serious adverse reaction of acute renal failure, Pruritus 1 (0.9%) 4 (3.5%), Alopeica 1 (0.9%) 2 (1.7%), Vomiting 13 (11.3%) 15 (13.0%), Physical Examination or Observational 3 (2.6%) 8 (7.0%), Elevated BUN (without creatinine)** 6 (5.2%) 0, Polydipsia 1 (0.9%) 4 (3.5%), Diarrhea or soft stool 6 (5.2%) 7 (6.1%), Eosinophilia was noted sporadically in the vehicle control, 1.1, and 5.3 mg/kg groups. Mild elevations in ALT values were noted sporadically in vehicle control, 3.2, and 5.3 mg/kg groups. On day 15, one cat in the 3.2 mg/kg group demonstrated a marked ALT elevation of 3397 U/L, with a markedly elevated AST of 3157 U/L. This finding was consistent with cystitis (mucosal urinary bladder hemorrhage, mottled-dark red appearance, and inflammation) which was frequently observed in all groups and occasionally affected the tail, tarsi or carpi, likely due to prolonged contact of the treated area to self-pettomising.

** Significant (p<0.0001) based on a two-sample t-test assuming equal variances. A 95% confidence interval for the difference between the two groups was calculated based on a two-sample t-test assuming unequal variances. A confidence interval of zero indicates no difference between the two groups.

The safety of mirtazapine for the management of weight loss in cats, 115 cats treated with vehicle control were evaluated for safety. The vehicle control was an ointment vehicle alone and the study included 116 cats treated with vehicle ointment administered topically to the inner pinna of the cat’s ear.

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2. Wet your gloved fingers, gently rub the ointment onto the site of application up to 4 mm (about 0.15 inch) in diameter. The device control is used for all animal studies.
3. The most common observations were ear pinnae reactions (erythema with or without blood and crusting) and a decrease in body weight.
4. The doses used in the target animal safety study were higher (2.8 to 5.4 mg) than the label dose. In the terminal study administering 5.3 mg/kg mirtazapine topically, histopathology showed chronic cholesterinic hyperplasia at the application site.

For a list of references, see page 1185. The study was conducted in 2005.

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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 a clinical study, Mirataz resulted in significant weight gain in cats in as little as 14 days following topical application of 2 mg per day
✔ Mirataz gives you a practical way to manage your patient’s weight loss without administration of oral medication and does not rely on the cat to eat to be medicated
✔ Formulated using proprietary Accusorb™ technology, Mirataz achieves measurable plasma concentrations of mirtazapine in cats
✔ Mirataz was safe both locally and systemically in a clinical study

“YOU REALIZE CATS DON’T REALLY HAVE 9 LIVES, RIGHT?”

For more information contact your KindredBio Sales Specialist at 1-888-608-2542, your preferred Distributor Sales Representative, or go to kindredbio.com/Mirataz

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