

Impact of Feline Weight Loss

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AAVSB RACE # 495-39814



Mirataz[®]
(mirtazapine transdermal ointment)



1

My cat family ...

- Marco & Polo
- Kevin & Stuart



2

Today's Discussion

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- Spotlight on cats
- Why worry about weight loss in cats?
- Recognizing feline weight loss
- Managing feline weight loss
- Why Mirataz?



3

Spotlight on Cats

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- There are an estimated 58.4M pet cats in the US¹
- Cats admitted to veterinary hospitals are more likely than dogs to be underweight
 - ~60% having recently lost weight²
- 9M cats present with weight loss annually^{3,4}
- 7M were NOT prescribed a medication to manage their weight loss prior to FDA approval of Mirataz^{3,4}

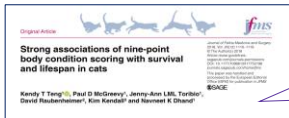


4

Why Does Weight Loss Matter?

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- Affects all ages & sizes of cats
- Early indicator of disease in geriatric cats⁵⁻⁷
- Slow onset – owners may not be concerned until other clinical signs
- Can lead to a poor body condition score – associated with decreased survival & lifespan in cats⁸



A retrospective study looking at the association between body condition score and survival and lifespan in cats. Found cats with a BCS < 6/9 had as much as 4.7 times higher risk of death.

5

Impact of Weight Loss

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Feline cancer patients' survival time significantly associated with weight and body condition score (BCS)⁹

- BCS < 5/9 median survival 3 months
- BCS 5/9 median survival 16 months

6

Cats are Unique Mirataz® (mirtazapine transdermal ointment)

Distinct health, medical, and diet requirements¹⁰⁻¹⁴

- Higher protein and amino acid requirement
- Digestive capabilities change with age
- Reduced ability to digest protein and fat
- Stable to increased metabolism with age
- Reduced ability to deal with dietary change or illness



7

Early Identification to Avoid Serious Consequences Mirataz® (mirtazapine transdermal ointment)

- Organ dysfunction¹⁵
 - Hepatic lipidosis
- Immune system dysfunction, poor wound healing, reduced strength^{11,16}
- Increased morbidity⁹ and mortality^{8,9}
- Prolonged hospitalization
 - Increased cost of care



Prolonged inadequate nutrition may be more detrimental to the patient than the primary disease process¹⁰

8

Impact on Human Animal Bond¹⁷ Mirataz® (mirtazapine transdermal ointment)

animals (IRDFP)

Factors Which Influence Owners When Deciding to Use Chemotherapy in Terminally Ill Pets

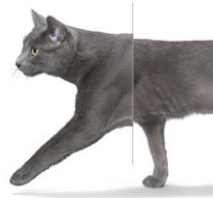
Jane Williams ^{1,2}, Catherine Phillips ³ and Hollie Marie Ryan ¹

Pet owners considered vomiting an acceptable side effect, but inappetence, weight loss, and depression unacceptable.



9

Recognizing Weight Loss



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10

The Chief Complaint

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Weight loss is a clinical sign – may be primary or secondary complaint

- "Losing weight" vs. inappetent, nausea, vomiting²⁸
- "Ain't Doing Right"

Early warning sign

- CKD
 - Median of 8.9% body weight loss 12 months before diagnosis⁷
 - Weight loss present 3 years prior to diagnosis⁷
- Cats with cancer, renal failure, and thyroid disease began to lose weight > 2 years before death⁶



Important to evaluate and trend body composition

11

Owner Awareness

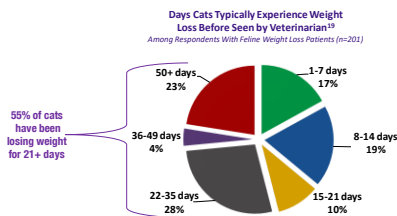
Mirataz[®]
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- Multi-cat households
- Free feeding or irregular feeding schedule
- Cats not handled regularly
- Long-haired cats
- Tummy "pooch"
- "Finally losing weight"



12

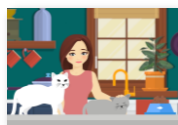
Owners Delay Seeking Treatment **Mirataz®**
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13

Asking Clients the Right Questions **Mirataz®**
(mirtazapine transdermal ointment)

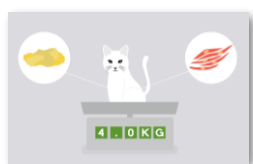
- How does your cat behave when he or she eats?
- Describe your cat's appetite.
- Describe your cat's eating behavior.
- How many times a day does your cat visit the food bowl?
- Describe your typical feeding routine with your cat.
- Tell me how your cat's eating habits have changed.



14

Body Composition Assessment **Mirataz®**
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1. Accurate body weight
2. Body Condition Score (BCS)
3. Muscle Condition Score (MCS)



15

Body Weight **Mirataz[®]**
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Weight loss = Loss of body weight

- Includes fat, muscle, and water (hydration)
- Relative to prior stable body weight
- A clinical study considered 1-2% weight change clinically relevant²⁰

Date	Weight
Aug 2017	4.0 kg
Feb 2018	3.5 kg
Mar 2018	2.9 kg
Apr 2018	2.5 kg

16

Body Condition Score (BCS) **Mirataz[®]**
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Assessment of Body Fat

- Lifespan decreased when cats had BCS < 5/9⁸
- Maximum BCS 3/9 = 4.7x risk of death⁹
- Maximum BCS 3/9 = 6.1x risk of shorter lifespan (cats 3-11 years of age)⁸

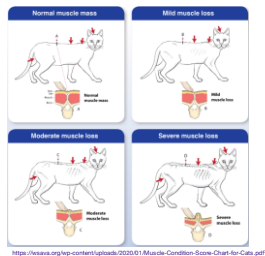


17

Muscle Condition Score (MCS) **Mirataz[®]**
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Assessment of Muscle Mass

- **Cachexia** = Disease-related loss of lean body mass and fat⁷
- **Sarcopenia** = Age-related loss of lean body mass⁷
- Loss of lean body mass is a significant risk factor for mortality⁹



18

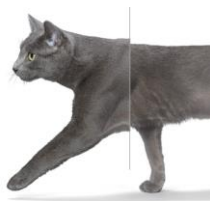
The Big Picture **Mirataz**[®]
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- Weight loss must be identified & addressed early⁷
 - Cachexia and sarcopenia are under-recognized by owners and veterinarians
- Poor body condition linked to reduced survival⁸
- Weight loss & anorexia impact owner perception of quality of life & influence euthanasia decisions^{7,23}
- Veterinarians often first to recognize change
- Owners rely on veterinarian's guidance for when & how to manage weight loss



19

Managing Feline Weight Loss



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20

Identify Underlying Cause & Support **Mirataz**[®]
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Early therapeutic intervention is essential to minimize the impact of weight loss while diagnosing the underlying cause.¹⁰

21

But in Real Life...

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A survey of US veterinarians indicated that

~9,000,000 CATS

PRESENT WITH WEIGHT LOSS /ANAPETENCE DUE TO UNDERLYING CONDITIONS¹

7 MILLION OF THOSE CATS WERE NOT PRESCRIBED A MEDICATION (compounded or human generic mirtazapine) to manage their weight loss^{1,2}

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 cats³

25

A Tough Pill to Swallow

Mirataz[®]
(mirtazapine transdermal ointment)

Human generic mirtazapine tablets have historically been used off-label

- Human tablets must be split or broken
- Inaccurate dosing shown to result in accidental overdose and toxicity²²
- Unknown user safety to people handling broken pills
- Unknown drug distribution in pill fragments
- Not ideal if cat is already inappetent, nauseous, or vomiting

Mirataz gives your clients and their cats the option for *one less* oral medication



26

Historical Use Of Mirtazapine

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Compounded liquid & transdermal mirtazapine used off-label

- Inconsistent mirtazapine in transdermal formulation²³
- Unproven safety and efficacy
- Unknown potency, purity, and stability
- Oral products placed on food only work if cat is eating and fed individually
- Liquids given by mouth may not be any easier than pilling

Drug exposure and clinical effect of transdermal mirtazapine in healthy young cats: a pilot study

Kofel K, Bennett, Lara R, Zaki, Paula K, Morgan, Sarah R, Brown, Ryan J, Hansen, Paul J, Langshofer, Luke A, Willenborg, Daniel L, Goodrich and Jessica W Quimby

BSAC

Compounded transdermal mirtazapine shown to result in variable and inconsistent gel concentrations.²³

27

Mirataz® (mirtazapine transdermal ointment)



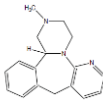
28

Now Available from Dechra!

Mirataz®
(mirtazapine transdermal ointment)

The FIRST and ONLY FDA-approved transdermal medication for the management of weight loss in cats

- Weight gain drug
- Multi-modal mechanism of action²⁴
- Orexigenic effect may be due to inhibition of serotonin receptors²⁴
- 2% transdermal ointment applied to inner pinna of ear
- 1.5 inch ribbon = 0.1 mL

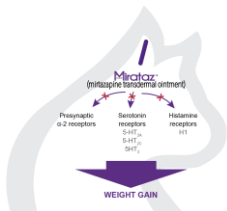


29

Mechanism of Action

Mirataz®
(mirtazapine transdermal ointment)

Mirtazapine is the active ingredient in Mirataz



30

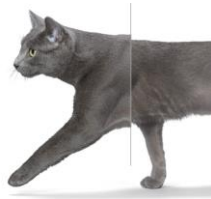
Mechanism of Action

Mirataz®
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31

Pharmacokinetics



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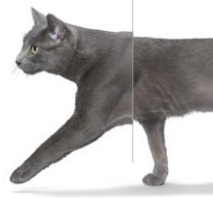
32

Mirataz®
(mirtazapine transdermal ointment)

Formulated using proprietary Accusorb technology,
Mirataz achieves measurable
plasma concentrations of mirtazapine.²⁵

33

Efficacy



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(mirtazapine transdermal ointment)

37

Clinical Field Study

Mirataz[®]
(mirtazapine transdermal ointment)

230 cats received treatment (safety population)³⁰

- 115 Mirataz : 115 placebo

224 cats in intent-to-treat (ITT) population^{31,32}

- 113 Mirataz : 111 placebo

177 cats in per protocol population^{30,32}

- 83 Mirataz : 94 placebo



Cats were required to have existing documented medical history of $\geq 5\%$ weight loss deemed clinically significant by the investigator³⁰

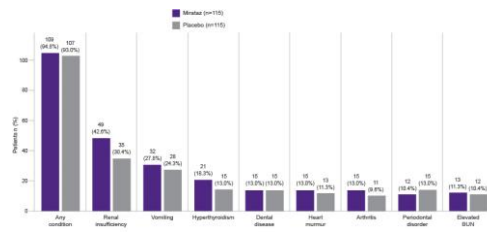
Mirataz or formulation with no active ingredient applied once a day for 14 days³⁰

38

Clinical Field Study

Mirataz[®]
(mirtazapine transdermal ointment)

PRE-EXISTING CONDITIONS AND RELEVANT MEDICAL HISTORY AT ENROLLMENT
(SAFETY POPULATION)³⁰



39

Safety – Clinical Field Study

Mirataz[®]
(mirazapine transdermal ointment)

230 cats in safety population (all cats treated in Mirataz [M] or placebo groups [P])

The most common adverse reactions included: application site reactions, behavioral abnormalities (vocalization and hyperactivity), and vomiting

- Application site erythema³⁰
 - 10.4% (M) vs 17.4% (P)
- Vomiting³⁰
 - 11.3% (M) vs 13.0% (P)
- Pre-existing vomiting³²
 - 27.8% (M) vs 24.3 % (P)



43

Safety – Clinical Field Study

Mirataz[®]
(mirazapine transdermal ointment)

ADVERSE EVENTS REPORTED DURING THE FIELD STUDY³¹

Adverse Reaction	Mirataz (n=115 [%])	Vehicle Control (n=115 [%])	Adverse Reaction	Mirataz (n=115 [%])	Vehicle Control (n=115 [%])
APPLICATION SITE (EAR PINNA)			PHYSICAL EXAMINATION OR OBSERVATIONAL		
Erythema	12 (10.4%)	20 (17.4%)	Itching	13 (11.3%)	15 (13.0%)
Crust/Scab	3 (2.6%)	6 (5.2%)	Dehydration	6 (5.2%)	5 (4.3%)
Redness	3 (2.6%)	6 (5.2%)	Diarrhea or soft stool	6 (5.2%)	7 (6.1%)
Swelling/Drainage	3 (2.6%)	3 (2.6%)	Heart murmur	5 (4.3%)	7 (6.1%)
Dermatitis or irritation	1 (0.9%)	9 (7.8%)	Inappetence	5 (4.3%)	5 (4.3%)
Allopice	1 (0.9%)	2 (1.7%)	Renal insufficiency	4 (3.5%)	0
Pruritus	1 (0.9%)	4 (3.5%)	Ear infection	3 (2.6%)	0
BEHAVIORAL			CLINICAL PATHOLOGY		
Vocalization	13 (11.3%)	2 (1.7%)	IgGemia	7 (6.1%)	1 (0.9%)
Hyperactivity	8 (7.0%)	1 (0.9%)	Elevated BUN (without creat- inine)	6 (5.2%)	0
Disoriented state or ataxia	4 (3.5%)	2 (1.7%)	Elevated creatinine and BUN	5 (4.3%)	1 (0.9%)
Lethargy/letharginess	4 (3.5%)	9 (7.8%)	Hyperepithelium	5 (4.3%)	0
Altered walking	3 (2.6%)	0	Hypokalemia	5 (4.3%)	2 (1.7%)
Aggression	2 (1.7%)	0	Pyria	5 (4.3%)	0
			Albumin	3 (2.6%)	5 (4.3%)
			Low urine specific gravity	3 (2.6%)	1 (0.9%)
			Monocytosis	3 (2.6%)	2 (1.7%)
			Neutrophilia	3 (2.6%)	2 (1.7%)

Elevated BUN levels not considered clinically relevant and likely due to increased incidence of renal disease at enrollment in the Mirataz group³²

44

Overall Safety

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(mirazapine transdermal ointment)

In a clinical study, Mirataz was safe both locally and systemically³²

Data supports the safe use of Mirataz when used as labeled³⁰



45

Application **Mirataz[®]**
(mirtazapine transdermal ointment)

Mirataz is applied topically once daily for 14 days, at a dosage of 2 mg/cat



- To be safe, wear disposable gloves when applying
- Avoid contact with the patient (human or animal) for 2 hours

Please see package insert for complete dosing and application instructions

46

Application Video **Mirataz[®]**
(mirtazapine transdermal ointment)



47

Important Safety Information **Mirataz[®]**
(mirtazapine transdermal ointment)

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 end of presentation.

48

Chronic Kidney Disease

Mirataz[®]
(mirtazapine transdermal ointment)

Inappetence, anorexia, nausea, vomiting → Progressive weight loss

CKD cat owner survey³⁶

- 43% abnormal appetite
- 52% needed to coax their cats to eat 5-7 days a week



Chronic kidney disease cats treated with mirtazapine gained significant weight.³⁸

49

Liver & Kidney Disease

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(mirtazapine transdermal ointment)

- Possible reduced metabolism with liver disease and reduced clearance with kidney disease, so concern for total drug exposure
- Elevated serum liver enzymes were noticed sporadically in the placebo and exaggerated dose groups in the target animal safety study
- Mirataz does not accumulate and is **not** nephrotoxic or hepatotoxic
- No requirement for treatment-related monitoring of blood work
- PK supports **daily** dosing
- Mirataz has lower C_{max} and AUC, important for this population of cats

50

Mirataz Summary

Mirataz[®]
(mirtazapine transdermal ointment)

- **FIRST & ONLY** FDA-approved transdermal medication for the management of weight loss in cats
- Significant weight gain in cats in as little as 14 days²⁴
- Orexigenic effect may be due to inhibition of serotonin receptors²⁴
- Proprietary Accusorb technology, achieves measurable plasma concentrations²⁵
- Safe both locally and systemically in clinical trial^{30,32}
- Use in cats with unintended weight loss associated with:
 - Underlying illness
 - Environmental factors

51

Impact of Weight Loss

Mirataz®
(mirtazapine transdermal ointment)

- ALL cats are at risk
- Early identification imperative
 - On average, cats presenting with weight loss have been losing weight for about a month¹⁹
- Treat weight loss proactively
- Monitor & manage body composition
 - Poor body condition impacts patient survival & lifespan⁸



52

Available Resources

Mirataz®
(mirtazapine transdermal ointment)

- Mirataz In-Clinic Resources
 - Cat Owner Brochure
 - Veterinary Detailer
 - Technical Bulletin
 - Videos
 - How to Apply Mirataz
 - Mechanism of Action
 - Recognition & Progression of Disease
 - Body & Muscle Composition
 - WSAVA BCS & MCS Posters
 - Mirataz.com
 - Dechra-us.com

- Free Online RACE-approved CE
dechra-us.com/academy



- Veterinary Technical Services Team
(866) 933-2472; support@dechra.com



53

Mirataz®
(mirtazapine transdermal ointment)

INDICATIONS: Mirataz is indicated for the treatment of depression and anxiety in cats.

CONTRAINDICATIONS: Mirataz is contraindicated in cats with known hypersensitivity to mirtazapine or any of the components of the ointment.

WARNINGS: Mirataz may cause sedation, dry mouth, and constipation. Monitor cats for these side effects.

ADVERSE REACTIONS: The most common adverse reactions observed in cats treated with Mirataz are sedation, dry mouth, and constipation.

HOW TO APPLY: Mirataz is applied topically to the skin of the cat. The ointment should be applied to a clean, dry, and hairless area of the skin.

DOSE: The recommended dose of Mirataz is 0.1 mg/kg body weight, applied once daily.

PHARMACOLOGY: Mirataz is a tetracyclic antidepressant that acts as a serotonin 2A receptor antagonist and a histamine H1 receptor antagonist.

PHARMACOKINETICS: Mirataz is rapidly absorbed after topical application and reaches its maximum plasma concentration within 2 hours.

STABILITY: Mirataz ointment is stable for 12 months when stored at room temperature.

HOW TO STORE: Store Mirataz ointment at room temperature (20°C to 25°C).

HOW TO DISPENSE: Mirataz ointment is available in 10 g and 30 g tubes.

HOW TO ORDER: Mirataz ointment is available through your local Dechra representative.

HOW TO CONTACT: For more information, please contact your local Dechra representative or call (866) 933-2472.

HOW TO REGISTER: Mirataz is a registered trademark of Dechra USA, Inc.

HOW TO PATENT: Mirataz is patented in the United States and other countries.

HOW TO TRADE: Mirataz is a trade name for mirtazapine transdermal ointment.

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54

Thank you everyone who stuck with me!
You are the best!!



Mirataz®
(mirtazapine transdermal ointment)

55



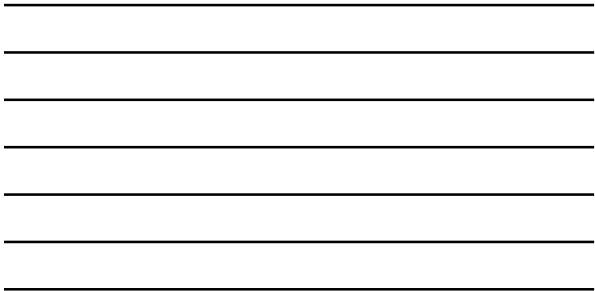
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Learn with
Dechra Academy.



56



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57

