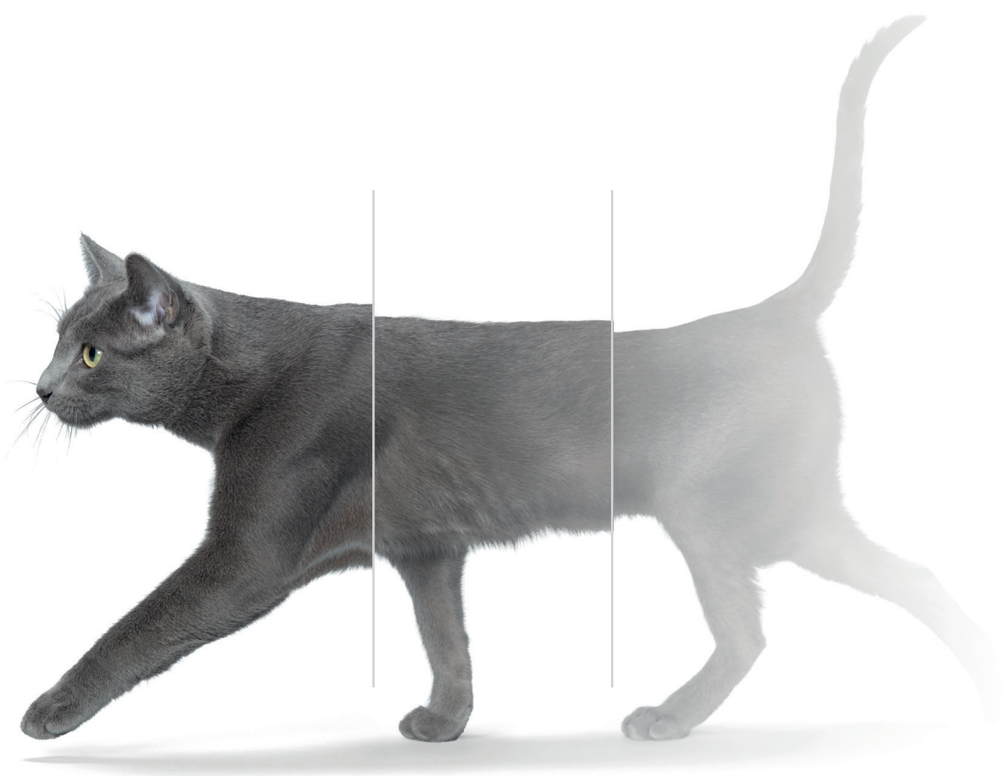
Dechra
Veterinary Products

Evaluation of Mirataz for Body Weight Gain in Cats



Mirataz®

Take control with Mirataz

BACKGROUND

On the 10/12/2019 pan European approval was gained for Mirataz, a **transdermal mirtazapine** ointment licensed for **body weight gain** in cats experiencing **poor appetite** and weight loss resulting from **chronic medical conditions**.

Mirtazapine is classified as a weight gain drug and has been used in cats as an appetite stimulant[1]. Appetite stimulation as a result of **oral** mirtazapine administration has been documented in both healthy cats[2] and those with chronic kidney disease[3]. The mechanism of action of mirtazapine is thought to be multifactorial, with **inhibition of type 2C serotonin receptors** and histamine receptors hypothesised as the reason for its orexigenic properties[4].

Success for **compounded** transdermal preparations in stimulating appetite in healthy cats has also been documented[5]. This method of application provides a **simple way for owners to apply medication** when faced with inappetence in their pet.

The purpose of this document is to review the findings of the pivotal field trial which led to the registration of Mirataz, in order to support your decision making when prescribing Mirataz.

STUDY DESIGN[1]

In a multi-centre, randomised, double-blind placebo controlled study, the difference in mean percent body weight gain (%BWG) was compared in cats treated with Mirataz (n= 83) to those receiving placebo (n = 94) (Per Protocol (PP) Population).

Inclusion criteria comprised:

1. ≥1 year old
2. ≥ 2 kg
3. Documented history of ≥5% bodyweight loss
4. Treatments which had no impact on the clinical conditions being investigated

Exclusion criteria comprised:

1. Pregnancy / lactation
2. Diagnosis of neoplasia or severe kidney disease
3. Administration of additional medications intended for weight gain within 7 days of the study
4. Cats that were not expected to survive the study

More information on the pre-existing conditions and concomitant medications documented in the study can be found in Tables 2 and 3.

Cats were dosed with 2 mg/cat Mirataz, or a placebo consisting of an identical formulation to Mirataz without the active ingredient, applied onto the inner pinna according to label recommendations. Effectiveness was defined as a combination of:

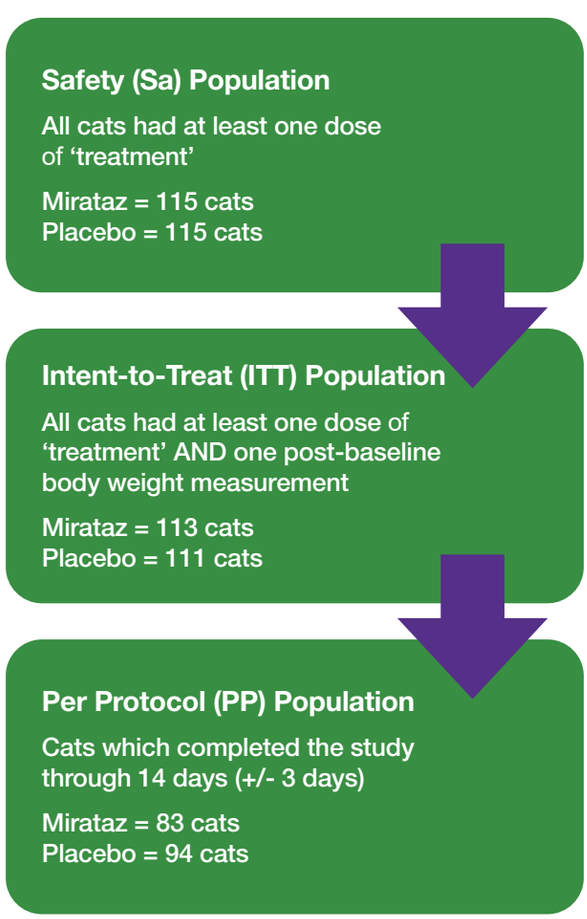
a) A statistically significant difference in mean %BWG between groups

b) A higher mean %BWG in the Mirataz group and

c) A mean %BWG in the Mirataz group ≥0

An explanation of the different populations referred to in the document is given in Figure 1 (right).

Figure 1. **STUDY POPULATIONS**



RESULTS

Efficacy

The mean percent change in bodyweight for cats receiving Mirataz was **+3.9%** compared to only +0.4% in the placebo group. This equated to a mean weight gain of **150 grams** in the Mirataz group versus only 10 grams in the placebo group. This change was considered **statistically significant** ($p < 0.0001$)[1].

Safety

Overall, the study found that there was **no significant difference in adverse events** (AEs) reported between the Mirataz and placebo groups[1].

The most common AEs documented included application site reactions, behavioural changes and vomiting[4]. Further details of adverse events can be found in Table 1[1].

Of the cats in the clinical field study (Sa Population), 27.8% in the Mirataz treated group had pre-existing vomiting at the time of enrolment due to underlying conditions[1].

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 enrolment in the Mirataz group[1].

Mirataz and Pre-existing Disease

Table 2 gives further details on the types and numbers of pre-existing conditions seen in cats within the field study, and Table 3 summarises the concomitant medications administered.

Where subcutaneous fluids were administered during the trial, body weight measurements had to be gained prior to administration, to ensure this did not influence results. Equally, for administration of corticosteroids, it was assured that the dose and schedule were not altered for 14 days prior to, or during, the study.

Table 2 highlights that **renal disease was the most common underlying condition** identified in cats enrolled on the study. Cats with suspect renal disease were a valuable inclusion in this study given their propensity for weight loss and inappetence, and a potential for delayed mirtazapine clearance in this population[8].

Further evaluation of study data for cats suspected of having renal disease showed that the mean %BWG results **reflected that of the overall group** and there was no significant difference between groups in incidence of overall adverse events or behavioural AEs of vocalisation and hyperactivity[9].

Table 1. Total incidence of adverse events (occurring in >5% of cats) [Sa population][1]

Adverse event	Mirtazapine (n = 115) n (%)	Placebo (n = 115) n (%)
Total Incidence	**70 (60.9%)**	**75 (65.2%)**
Vomiting	13 (11.3%)	15 (13.0%)
Vocalisation (including crying, meowing)	13 (11.3%)	2 (1.7%)
Application site erythema[a]	12 (10.4%)	20 (17.4%)
Hyperactivity (including pacing, restlessness, sleeplessness)	8 (7.0%)	1 (0.9%)
Haematuria	7 (6.1%)	1 (0.9%)
Diarrhoea or soft stool	6 (5.2%)	7 (6.1%)
Dehydration	6 (5.2%)	5 (4.3%)
Elevated BUN (without creatinine)	6 (5.2%)	0
Heart murmur	5 (4.3%)	7 (6.1%)
Lethargy (including depressed, sedation, weakness)	4 (3.5%)	9 (7.8%)
Anaemia	3 (2.6%)	8 (7.0%)
Application site residue	3 (2.6%)	8 (7.0%)
Application site crust/scab	3 (2.6%)	6 (5.2%)
Application site dermatitis or irritation[a]	1 (0.9%)	9 (7.8%)

[a]Application site dermatitis as defined by the clinical investigator and application site erythema as defined by reddening or discoloration not classified by the clinical investigator as dermatitis or irritation.

Table 2. Pre-existing conditions of cats enrolled categorised by body system affected (Sa population)[6]

Pre-existing Condition	Mirtaz (n = 115) n (%)	Placebo (n = 115) n (%)
Renal	64 (55.7%)	48 (41.7%)
Multisystemic	56 (48.7%)	48 (41.7%)
Dental	35 (30.4%)	39 (33.9%)
Gastrointestinal	31 (27.0%)	35 (30.4%)
Cardiovascular	25 (21.7%)	25 (21.7%)
Endocrine	24 (20.9%)	19 (16.5%)
Urinary	23 (20.0%)	32 (27.8%)
Musculoskeletal	22 (19.1%)	14 (12.2%)
Skin and aural	20 (17.4%)	15 (13%)
Behavioral	11 (9.6%)	16 (13.9%)
Respiratory	8 (7.0%)	17 (14.8%)
Hepatobilliary	8 (7.0%)	4 (3.5%)

Table 3: Concomitant medications administered (occurring in >3% of cats in any treatment group [Sa population])[7]

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

CONCLUSION

The study showed that **Mirataz is effective** in cats suffering from weight loss resulting from **underlying medical conditions**[4] after 14 days of daily application. The study found that topical application is **well tolerated**, and resulted in **significant weight gain** in treated cats vs placebo[1].

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MIRATAZ: Mirataz contains Mirtazapine UK: POM-V **IE:** POM

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