

EFFICACY REVIEW

PRODUCT: CERTIFECT
DATE: February 1, 2011
FILE SYMBOL: 65331-T
DP BARCODE: DP 386346
DECISION: 423378
GLP: No
CHEMICALS: Fipronil (9.8%) + (S)-Methoprene (8.8%) + Amitraz (22.1%)
CHEMICAL NUMBERS: Fipronil - 129121 (S)-Methoprene - 105402 Amitraz - 106201
PURPOSE: To determine efficacy for the label claim “*Effective after exposure to sunlight*” on a new registration for a spot-on combination product for dogs.

MRIDs:

48342901. A Study to Evaluate ML-3,481,564 in the prevention of the Transmission of Ehrlichia canis (Dumler et al., 2001) from Infected Rhipicephalus sanguineus (Latreille, 1806; Acari: Ixodidae) to Dogs under Natural Conditions.

48342902. A Study to Evaluate ML-3,481,564 in the prevention of the Transmission of Babesia canis (Piana & Galli-Valerio, 1895) from Infected Dermacentor reticulatus (Fabricius, 1794) to Dogs under Natural Conditions.

TEAM REVIEWER: Autumn Metzger

EFFICACY REVIEWER: Autumn Metzger, M.S.

Autumn Metzger 2/1/11

SECONDARY EFFICACY REVIEWER:

Joanne Edwards, M.S.

Joanne Edwards 2/1/11

BACKGROUND

CERTIFECT is a topical spot-on insecticide treatment for the control of fleas and ticks for dogs and puppies 7 weeks of age and older. The product is applied on the skin between the shoulder blades once monthly. This product is similar to the already registered product, Frontline Plus with the addition of the chemical amitraz for added tick efficacy. These studies were submitted to support the claim “*Effective after exposure to sunlight.*”

Labeled Application Rates:

Dog Size	Application Rate
Dogs & Puppies older than 7 weeks and up to 22 lbs	.036 fl oz
Dogs 23-44 lbs	.072 fl oz
Dogs 45-88 lbs	.145 fl oz
Dogs 89-132 lbs	.217 fl oz

DATA REVIEW

The following data review is comprised of explanations of materials and methods, and a summation of experimental results containing tables with reformatted data.

48342901. A Study to Evaluate ML-3,481,564 in the prevention of the Transmission of *Ehrlichia canis* (Dumler et al., 2001) from Infected *Rhipicephalus sanguineus* (Latreille, 1806; Acari: Ixodidae) to Dogs under Natural Conditions.

Objective

The trial objective was to evaluate the efficacy of combination product ML-3,481,564 (Frontline plus + amitraz) against the transmission of *Ehrlichia canis* from the brown dog tick when given monthly to dogs in natural (non-lab) settings. For the purpose of our review the objective it to prove efficacy of the product to dogs exposed to sunlight.

Set Up

Thirty dogs were split into 2 groups of 15 dogs each. Groups 1 was a non-treated control and group 2 were treated monthly up to day 113. Dogs were housed in indoor/outdoor runs consisting of a 50 m² outdoor area and a 12 m² covered shelter area. As per verified in an email from Tim Dotson on 1/25/11 dogs had free access to either area and were exposed continuously to severe natural tick pressures.

Results

No actual tick counts were conducted, only diagnosis of *E. Canis* via IFI or DNA PCR testing. Twelve out of 15 (80%) of the control dogs were IFI positive for *E. Canis* vs. 3/15 (20%) of the treated dogs (p= .003). Thirteen out of 15 dogs (87%) were DNA PCR positive for *E. Canis* vs. 5/15 (33%) in the treated group (p=.008). Nine of the 15 control dogs ended up dying from *E. Canis* conditions.

Conclusion

Treated dogs showed significant (p<.05) efficacy over non-treated controls in preventing *E. Canis* transmission during intense natural tick challenges. Depending on the testing used, 20-33% of treated dogs still were positive for the *E. Canis* strain.

48342902. A Study to Evaluate ML-3,481,564 in the prevention of the Transmission of *Babesia canis* (Piana & Galli-Valerio, 1895) from Infected *Dermacentor reticulatus* (Fabricius, 1794) to Dogs under Natural Conditions.

Objective

The trial objective was to evaluate the efficacy of combination product ML-3,481,564 (Frontline plus + amitraz) against the transmission of *Babesia canis* from the ornate dog tick when given monthly to dogs in natural (non-lab) settings. For the purpose of our review the objective it to prove efficacy of the product to dogs exposed to sunlight.

Set Up

Twenty dogs were split into 2 groups of 10 dogs each. Groups 1 was a non-treated control and group 2 were treated monthly up to day 196. Dogs were housed in indoor/outdoor runs consisting of a 50 m² outdoor area and a 12 m² covered shelter area. As per verified in an email from Tim Dotson on 1/25/11 dogs had free access to either area. Each dog was walked for at least 2 hours once weekly to expose them to ticks in an area known to harbor ornate dog ticks positive for *B. canis*. Ticks were counted weekly on each dog.

Results

No ticks were found on any of the treated dogs at any time in the study providing a 100% efficacy. For the control group, there were some days that none or very few ticks were found on any dog, however for 13 of the 21 tick count days the treated groups showed significant ($p < .05$) efficacy vs. the untreated control in the natural challenges.

Conclusion

Treated dogs showed significant ($p < .05$) efficacy over non-treated controls in tick counts of the ornate dog tick.

RECOMMENDATIONS:

Current claims and recommendations as they relate to the efficacy studies on ticks:

CLAIM- *Effective after exposure to sunlight*

The combination of the weight-of-evidence provided in these two submitted studies, as well as data provided originally for the product, Frontline Plus (Fipronil + (S)-Methoprene) will support this label claim.

EFFICACY REVIEW

PRODUCT: CERTIFECT

DATE: January 20, 2011

FILE SYMBOL: 65331-T

DP BARCODE: D 384674

DECISION: 423378

GLP: N/A


CHEMICALS: Fipronil (9.8%) + (S)-Methoprene (8.8%) + Amitraz (22.1%)

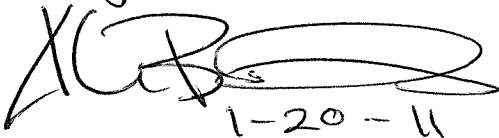
CHEMICAL NUMBERS: Fipronil - 129121 (S)-Methoprene - 105402 Amitraz - 106201

PURPOSE: To respond to rebuttal submitted December 17, 2010 by Merial for Agency review dated November 3, 2010 (DP Barcode 372045)

MRIDS: N/A

TEAM REVIEWER: Autumn Metzger

EFFICACY REVIEWER: Autumn Metzger, M.S.  1/20/11

SECONDARY EFFICACY REVIEWER: Kable Bo Davis, M.S.  1-20-11

BACKGROUND:

CERTIFECT for dogs (EPA File Symbol 65331-T) is intended for the control of fleas and ticks infesting dogs and puppies eight weeks of age and older.

Agency review dated November 3, 2010 (D423378) contained the following recommendations as they relate to the rebuttal submitted:

Claim 1 - "Provides synergistic efficacy against ticks"

Due to heightened efficacy implications, the claim is unacceptable.

Label Recommendation – delete all

Claim 2 –Long lasting

This claim is not qualified. In addition, claims for efficacy should coincide with label application recommendations and therefore should not be greater than 30 days for ticks, as is the instructed time for re-application.

Label Recommendation – delete or qualify this claim to read “Lasts 30 days” to coincide with application instructions.

Claim 3 –Rapid, Rapidly, Quick, Quickly, Fast, Fast Acting

These are not qualified claims nor is there data to support any of such claims.

Data supports the label claim “starts killing ticks in 12 hours,” which is not considered “quick” or “rapid.”

Label Recommendation – delete all, may replace with Label “starts killing ticks in 12 hours.”

Claim 5 - Effective after exposure to sunlight

There were no data submitted for this claim.

Label Recommendation – delete all such claims.

Claim 6 - Prevents attachment of ticks, Prevents tick feeding

There were no data submitted for this claim.

Label Recommendation – delete all such claims.

RECOMMENDATIONS:

Current recommendations as they relate to the rebuttal submitted by Merial on December 17, 2010:

Claim 1 - "Provides synergistic efficacy against ticks"

For the purpose of pesticides, the term “synergistic” refers to an effect where one active ingredient is enhanced by another chemical, which does not have any pesticidal effects itself. Since fipronil is also an active ingredient for this product, killing both fleas and ticks itself, it would not fit into this category. The term rather would be called “potentiation,” which in place could be used as a label claim if desired.

Claim 2 –Long lasting

This claim can be kept on the label only if qualified to coincide with application instructions. An acceptable claim is: “Long lasting for 30 days.”

Claim 3 –Rapid, Rapidly, Quick, Quickly, Fast, Fast Acting

These claims may only be kept if qualified. The best data submitted supports claims for “Rapid, Rapidly, Quick, Quickly, Fast, Fast Acting in 18 hours” or “Starts killing in 6 hours.”

Claim 5 - Effective after exposure to sunlight

These claims may be added back on after being supported by bridging data for original product Frontline Plus in addition to recently submitted studies MRIDs 48342901 & 48342902, which were reviewed under DP 386346, dated February 1, 2011.

Claim 6 - Prevents attachment of ticks, Prevents tick feeding

The following claims were never proven or supported by weight of evidence in any data submitted. As these claims are very difficult to prove, the Agency suggests submitting a protocol review for a new study to see if there would be a data design that may be able to prove such claims.

Claim 8 - Rapidly kills all stages of ticks

This claim can be kept with the following revision: “Rapidly kills all stages of ticks in 18 hours” or “Starts rapidly killing ticks in 6 hours.”

Claim 10 - 3-way protection against fleas, ticks and chewing lice

This claim can be kept.

Claim 11 - Starts killing ticks within 2 hours

This claim can be kept if revised to read: “Starts killing ticks within 6 hours” as supported by the submitted data.

In the rebuttal it was noted that the 2 hour claim was supported by MRID 47914225, however that data showed that the tick challenge was done over 24 hours after treatment, therefore not supporting a “2 hour claim” but rather a 26 hour claim.

Claim 13 - Proven treatment technology

This claim can be kept.