

11556-127

4/29/2010

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460



APR 29 2010

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Douglas Spilker, Ph.D
Bayer HealthCare LLC, Animal Health Division
P.O. Box 390
Shawnee Mission, KS 66201-0390

Dear Dr. Spilker:

Subject: Review new Child Resistant Packaging studies (CRP), amend the opening instructions on the label per the CRP studies submitted and change the primary brand name
Advantage II Large Dog
EPA Registration No. 11556-127
Decision No. 424616

The labeling referred to above submitted in connection with the Federal Insecticide, Fungicide and Rodenticide, as amended, is acceptable with the following comments and conditions:

Label Comments:

1. The primary brand name change from "Advantage Plus 55 for Dogs" to "Advantage II Large Dog" is acceptable.
2. On page 4, under "Additional Information," revise the sentence that reads "Treatment of dogs with Advantage II rapidly kills fleas which condition" to read "Treatment of dogs with Advantage II rapidly kills fleas within 12 hours whichcondition" to qualify "rapidly."
3. On page 4, under "Additional Information," revise the sentence that reads "Advantage II kills adult fleas quickly, inhibits... adult stage" to read "Advantage II kills adult fleas quickly within 12 hours, inhibits....adult stage" to qualify "quickly."
4. On page 4, under the "Storage and Disposal" section, revise the subheadings to read: **"Pesticide Storage"** and **"Pesticide Disposal and Container Handling."**
5. On page 6, under "Optional Marketing Claims," revise the claim that reads "Starts working by contact" to read "Starts working through contact."

6. On page 7, under "Optional Marketing Claims," revise the claim that reads [Dual-Action] [2-way] formula" to qualify what is meant by "dual-action" and "2-way."
7. On page 7, under "Optional Marketing Claims," revise the claim that reads "Dual protection (against fleas and lice)" to read "Dual protection against fleas and lice" to qualify what is meant by "dual protection."

Conditions of acceptance:

1. This registration is now time-limited and expires two years from the date this product is first released for shipment.

You must provide the Agency with a projected release for shipment at least 30 days in advance.
2. Only one basic confidential statement of formula will be on file for this product at any one time; no alternate formulations or minor formulation amendments will be submitted or approved for this product.
3. You must submit quarterly enhanced incident reports and quarterly sales information in doses sold for this product beginning [January 1, April 1, July 1, or October 1, whichever date most closely follows the release for shipment date.]

Please flag any Confidential Business Information as such. Enhanced incident reporting should be submitted to the Product Manager. Quarterly sales information should be submitted to the Registration Division, Immediate Office (attn: Kimberly Nesci).

The following is a list of information that must be included in the quarterly reports for each incident:

EPA Registration Number
Product name (brand name)
Lot #
Where purchased: internet, store, veterinarian
Active Ingredient(s)
Weight range for product

Date on which incident occurred. (mm/dd/yyyy)
State in which the incident occurred. (standard 2 letter abbreviation)
Registrant case #

Species: dog, cat, other (specify)
Breed: (as reported by pet owner)
Age: months or years
Sex: M, F, or neutered
Weight: pounds

Primary Route of Exposure: dermal, oral, other animal, inhalation, other
 Body System: neurological, dermatological, GI, respiratory, ocular, other
 Major signs noted with separate column for each sign, using standard terminology
 Time to Onset: (hours, days)
 Treated by veterinarian: yes or no
 First time product used: yes or no
 Misuse: use on incorrect species, overdose, too frequent dosing, other (describe)
 Any known precondition
 EPA Severity Code: death, major, moderate, minor
 Outcome: died, recovered, still treated, unknown

4. Along with the enhanced incident reporting, you must submit an analysis of the incidents seen, to include the following details:

- All incidents should be reported including all minor dermal and ocular irritation reports.
- Summary table for dogs showing number of incidents of each severity code for each route of exposure. Each incident should only be reported once. If one incident has several routes of exposure, the order should be ocular > oral > dermal. In other words, an incident with both oral and dermal exposure would be reported as oral exposure, and an incident with both ocular and oral exposure would be reported as ocular exposure.
- A similar summary table for cats (misuse or secondary exposure) showing number of incidents of each severity code for each route of exposure.
- Summary table for dogs and table for cats showing number of incidents that are believed due to secondary exposure (e.g., multi-pet households).
- A summary table for dogs showing number of incidents for each severity code for these age ranges: <3 months, 3-6 months, 6-9 months, 9-12 months, 1 yr, 2 yr, 3 yr, 4 yr, 5 yr, 6 yr, 7 yr, 8 yr, 9 yr, 10 yr, 11 yr, 12 yr, 13 yr, 14 yr, 15 yr, >15 yr.
- A summary table showing the number of dog incidents for each severity code for each pet weight range on the product label.
- A summary table for dog weight showing number of incidents for each product weight range. This table should show number of incidents in dogs weighing less than that product weight range, number of incidents in dogs in lower half of weight range, number of incidents in dogs in upper half of weight range, and dogs weighing more than the product weight range.
- Table showing number of incidents for each dog breed.

- Table showing number of incidents in dogs for each clinical sign.
- Table showing number of incidents in dogs for each organ system.
- Report aggregate incidents, but do not combine moderate and minor incidents.

If EPA determines that future mitigation measures are necessary for all pet spot-ons, the Agency will inform registrants. If mitigation measures are necessary, EPA may take regulatory action.

Two copies of the finished labeling must be submitted prior to releasing the product for shipment. If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA sec. 6(e). Your release for shipment of the product constitutes acceptance of these conditions. A copy of your label stamped "Accepted with Comments" is enclosed for your records. If you have any questions regarding this label, please contact Autumn Metzger at (703) 305-5314.

Sincerely,



Venus Eagle
Product Manager 01
Insecticide-Rodenticide Branch
Registration Division (7505P)

50f/2

Reason To Issue: Minor updates and change primary brand name. Date: 04/28/10
Supersedes: 12/07/09

NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

Advantage® II Large Dog

Once-A-Month Topical Treatment for Fleas and Lice
On Dogs and Puppies 7 Weeks and Older and Weighing 21-55 lbs.

READ ENTIRE LABEL BEFORE EACH USE

For the Prevention and Treatment of Flea and Lice Infestations [on Dogs]

[Selected optional claims bulleted here from page 6 and/or 7]

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ACCEPTED
With COMMENTS
In EPA Letter Dated:
APR 29 2010
Under the Federal Insecticide, Fungicide
and Rodenticide Act, As amended, for the
pesticide Registered under EPA Reg. No:
11556-127

<u>Active Ingredients</u>	<u>% By Weight</u>
Imidacloprid	9.10%
Pyriproxyfen	0.46%
Other Ingredients.	<u>90.44%</u>
Total.	100.00%

EPA Reg. No. 11556-127

EPA Est. 11556-DEU-1

KEEP OUT OF REACH OF CHILDREN

CAUTION

[See back panel for First Aid]

[For Directions For Use, and Storage and Disposal (instructions),
See supplemental labeling inside]

Reason To Issue: Minor updates and change primary brand
name.

Date: 04/28/10
Supersedes: 12/07/09

60912

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS

Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling.

HAZARDS TO DOMESTIC ANIMALS

For external use only. Do not use on puppies under 7 weeks of age. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing animals. Individual sensitivities, while rare, may occur after using ANY pesticide product for pets. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product. For consumer questions call 1-800-255-6826. For medical emergencies call 1-800-422-9874.

FIRST AID

Have the product container or label with you when calling a poison control center or doctor, or going for treatment.

IF SWALLOWED: Call a Poison Control Center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything to an unconscious person.

IF IN EYES: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.

IF ON SKIN: Wash with plenty of soap and water.

TO PHYSICIAN: Treat the patient symptomatically.

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.

70x12

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name.

Date: 04/28/10
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HOW TO OPEN

1. Being careful not to cut close to the blister cavities, take scissors and cut off one section of the card containing a single tube.
2. Take the separated section, and cut into the blister cavity across the small side, close to the cap of the tube.
3. Peel off the foil, and take out the tube.
4. Repeat steps 1 to 3 for each tube.



HOW TO APPLY

1. Use only on dogs. Do not use on other animals.
2. Remove one applicator tube from the package. See "HOW TO OPEN" section.
3. Hold applicator tube in an upright position. Pull cap off tube.

[Visuals Depicting How to Open Applicator Tube]

4. Turn the cap around and place other end of cap back on tube.
5. Twist cap to break seal, then remove cap from tube.

[Visuals Depicting Application To Animal]

6. The dog should be standing for easy application. Apply the entire contents of the tube evenly to three or four spots on the top of the back from the shoulder to the base of the tail. At each spot, part the hair until the skin is visible. Place the tip of the tube on the skin and gently squeeze to expel a portion of the solution on the skin. Do not apply an excessive amount of solution at any one spot that could cause some of the solution to run off the side of the dog. Do not get this product in your pet's eyes or mouth.

80f12

Reason To Issue: Minor updates and change primary brand name.

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7. Discard empty tube as described in the Storage and Disposal section.
8. Under normal conditions the product is effective for a month. However, in case of severe flea infestation, retreatment may be necessary earlier than four weeks. Do not re-treat more often than once every seven (7) days. After flea control is obtained, return to a monthly retreatment schedule.

ADDITIONAL INFORMATION

The successive feeding activity of fleas on dogs frequently elicits a hypersensitivity skin disorder known as flea allergy dermatitis (FAD) or flea bite hypersensitivity. Treatment of dogs with Advantage® II rapidly kills fleas which may reduce the incidence of this condition.

Advantage® II kills existing fleas on dogs within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting for four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Fleas, flea eggs, and flea larvae in the dog's environment are killed following contact with an Advantage® II treated pet. Advantage® II provides multi-stage flea control effectively breaking all flea life-cycle stages for quick and lasting control of flea populations.

Advantage® II kills adult fleas quickly, inhibits the development of immature flea life stages and prevents them from reaching the biting adult stage.

Advantage® II kills [(biting) (chewing)] lice that infest dogs and puppies, and prevents further infestations.

Advantage® II is waterproof and remains effective following a shampoo treatment, swimming or after exposure to rain or sunlight.

Monthly treatments are required for optimal control and prevention of fleas.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Storage: Store in a cool, dry place.

Disposal: Nonrefillable container. **If empty:** Do not reuse or refill this container. Place in trash or offer for recycling if available.

If partly filled: Call your local solid waste agency or 1-800-422-9874 for disposal instructions. Never place unused product down any indoor or outdoor drain.

Reason To Issue: Minor updates and change primary brand
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90412
Date: 04/28/10
Supersedes: 12/07/09

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Bayer HealthCare LLC, Animal Health Division warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. To the extent consistent with applicable law, any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc.

Net Contents: ([One][Four] [Six]) 0.084 fl. oz. (2.5 mL) Tubes

EPA Est. 11556-DEU-1
EPA Reg. No. 11556-127

Manufactured for
Bayer HealthCare LLC
Animal Health Division
P.O. Box 390
Shawnee Mission, Kansas 66201 USA

Made in Germany

Reason To Issue: Minor updates and change primary brand name.

Date: 04/28/10
Supersedes: 12/07/09

NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

OPTIONAL MARKETING CLAIMS

- For use on dogs and puppies 7 weeks of age and older
- Advantage II contains [imidacloprid], and [an/the] [insect growth regulator] [IGR] [pyriproxyfen]
- A single topical application remains effective for [4 weeks] [a month]
- Convenient, easy to apply topical solution
- Convenient, easy to apply and fragrance free [monthly] [topical solution]
- Once a month topical flea treatment for dogs 7 weeks of age or older
- Advantage II is indicated for the prevention and treatment of fleas on dogs 7 weeks of age and older
- For the treatment and prevention of flea [and lice] infestations
- One treatment prevents further flea infestations for [4 weeks] [a month]
- Kills fleas on dogs within [12] hours and continues to prevent infestations for [four weeks] [a month]
- Kills fleas before they lay eggs
- Larval flea stages in the dog's environment are killed following contact with an Advantage II treated dog
- Kills larval stages of fleas in the dog's environment
- Kills fleas within [12] hours of application
- Stops existing flea infestations by killing adult fleas
- Prevents [Stops] reinfestations by killing adult fleas before they lay eggs
- [Prevents] [Stops] flea eggs from hatching [into biting adults]
- Effectively breaks the flea life cycle
- Effectively targets all [life] stages of [fleas]
- [Kills] [Controls] all flea life stages
- 3-way flea protection ([kills] [controls] adults, larvae, and eggs)
- [Prevents] [Stops] flea eggs [and flea larvae] from developing into [(biting) (adult)] fleas
- Treatment with Advantage II rapidly kills fleas which may cause flea allergic dermatitis [FAD] or flea bite hypersensitivity
- Flea adulticide, larvicide, and oocide
- Kills flea eggs
- Controls highly [irritating] [annoying] [flea] [insect] bites
- Controls flea problems
- Provides flea protection
- Controls existing fleas and flea eggs [(plus) (and)] [prevents] future flea infestations in the home
- Starts working by contact

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- [Dual-Action][2-way] formula
- Use flea [prevention][protection] year-round
- Contains an insect growth regulator (IGR) to kill flea eggs and prevent re-infestation
- Monthly use of Advantage II kills fleas which may cause ([flea allergy dermatitis][flea bite hypersensitivity])
- Multi-stage flea control
- Prevents fleas on treated dogs from infesting (reinfesting) your home
- Kills fleas which may serve as intermediate hosts for tapeworms
- Kills [(biting) (chewing)] lice
- For treatment and prevention of [(biting) (chewing)] lice [infestations]
- Stops existing [(biting) (chewing)] lice infestations
- Dual protection (against fleas and lice)
- Treats, prevents and controls [(biting) (chewing)] lice [infestations]
- Provides effective control of [(biting) (chewing)] lice [infestations]
- Kills [(biting) (chewing)] lice and prevents further infestations
- For treatment and prevention of infestations with [(biting) (chewing)] lice
- Remains effective after bathing and/or swimming
- Remains effective following swimming and/or shampooing
- Waterproof
- Remains effective after exposure to rain or sunlight
- Fragrance free
- [In child-resistant packaging]

120912

Reason To Issue: Minor updates and change primary brand
name.

Date: 04/28/10
Supersedes: 12/07/09

(Label on Individual Tube)

Advantage[®] II Large Dog

9.10% Imidacloprid

0.46% Pyriproxyfen

0.084 fl. oz. (2.5 mL)

EPA Reg. No. 11556-127

CAUTION

Keep Out of Reach of Children

Read The Entire Label Before Use

BAYER

Lot No. 0000000