

PRODUCT MONOGRAPH

KWELLADA-P CREME RINSE

Permethrin Crème Rinse 1% w/w

Topical Pediculicide and Ovicide

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Date of Preparation: June 26, 2012

Control Number: 156218

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KWELLADA-P CREME RINSE
Permethrin Crème Rinse 1% w/w

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Non-medicinal Ingredients
For External Use Only	Kwellada-P Crème Rinse (1% Permethrin cis/trans ratio of 25:75) is available in plastic bottles containing 50 mL and 200 mL crème rinse.	It also contains isopropyl alcohol, propylene glycol, stearylalkonium chloride, lauryl alcohol, polyoxyethylene 4 lauryl ether, triethylamine, polyquaternium -10 and Carbomer 980.

INDICATIONS AND CLINICAL USE

Kwellada-P Crème Rinse is indicated for the treatment of *Pediculus capitis*, including adults, nymphs and eggs. One application of Kwellada-P Crème Rinse is usually adequate to eradicate the infestation of head lice. Should re-infestation occur, or the first application does not completely eradicate the head lice, a second treatment should be administered seven days after the initial treatment.

Geriatrics (> 65 years of age):

No data available

Paediatrics (< 2 years of age):

No data available.

CONTRAINDICATIONS

Kwellada-P Crème Rinse is contraindicated in patients with a known sensitivity or reaction to permethrin, any components of the product, other pyrethroids or pyrethrins excipients or to

chrysanthemums.

WARNINGS AND PRECAUTIONS

Kwellada-P Crème Rinse is for use when live lice or their eggs are present. It is not for prophylactic/regular use to prevent head lice.

Kwellada-P Crème Rinse should be discontinued if hypersensitivity occurs.

For external use only.

It is important to ensure that the course of treatment is followed as directed because treatment failure has been reported when this has not occurred.

General

Permethrin is not an eye irritant, but contact with the eyes should be avoided because other components of the products may cause marked irritation. If Kwellada-P Crème Rinse comes in contact with the eyes it can cause irritation. If this occurs, the eyes should be rinsed. In the event of accidental ingestion of Kwellada-P Crème Rinse, please seek immediate medical attention. During head lice infestation the scalp and surrounding skin are often irritated resulting in erythema, edema and frequently pruritus. These symptoms can be exacerbated after treatment. If skin irritation occurs and does not improve, consult a doctor. If applying routinely, wear gloves to avoid irritation.

Special Populations

Pregnant Women:

Safety has not been established during controlled clinical trials for use in pregnant women. Kwellada-P Crème Rinse should be used when the expected benefits outweigh the potential risks.

Nursing Women:

Because it is not known whether permethrin is excreted during lactation consideration should be given to discontinuing nursing during treatment with Kwellada-P Crème Rinse or withholding treatment if it is not possible to discontinue nursing.

Paediatrics (<2 years of age):

Kwellada-P Crème Rinse is safe and efficacious in children over two years of age. The safety and efficacy of permethrin has not been established in children under the age of two years. Do not use on children under 2 years of age.

Geriatrics (> 65 years of age):

No data available.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Clinical Trial Adverse Drug Reactions

Clinical trials have indicated that adverse reactions are reported infrequently. Adverse reactions which do occur are usually mild and resolve rapidly. They are local in nature.

In clinical trials pruritus was the most frequently reported adverse event with fewer than 3% of patients reporting it. The next most frequently reported adverse event was burning and stinging followed by erythema which was reported by less than 1% of patients.

Other reported adverse events include paraesthesia, eczema, skin oedema, rash, skin irritation, skin discomfort, smarting, and pain of skin.

DRUG INTERACTIONS

Overview

No data available.

DOSAGE AND ADMINISTRATION

For external use only. Do not apply to mucous membranes, or near the eyes. Do not use on children under 2 years of age. Keep out of sight and reach of children.

After the hair has been shampooed, rinsed and toweled dry, apply enough Kwellada-P Crème Rinse to saturate the hair and scalp, between 25 to 50 mL. Leave on for 10 minutes. The crème rinse should then be thoroughly rinsed off with water and the hair toweled dry. Nits can be combed out with the comb provided, if desired.

One treatment is usually adequate to eliminate the head lice.

Kwellada-P Crème Rinse should be shaken before use.

OVERDOSAGE

There has been no incidence of ingestion of Kwellada-P Crème Rinse.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Symptoms of overdose may include dizziness, loss of appetite, nausea, vomiting, headache, weakness, seizures, and loss of consciousness.

ACTION AND CLINICAL PHARMACOLOGY

Permethrin, a synthetic pyrethroid, has a broad spectrum of insecticidal activity combined with high potency when applied topically to insects, including head lice, *Pediculus capitis*.

Like other pyrethroids, permethrin is a sodium channel toxin. In susceptible nerve cells small amounts of permethrin cause a change in the kinetics of the sodium channel. Although the activation of the sodium current is unaffected, the rate of inactivation of the current is greatly slowed. This tail current, even at low doses, is adequate to cause repetitive activity. One normal action potential, in the presence of permethrin, leads to a series of abnormal action potentials. Consequently, there is repetitive firing of the neuron.

Studies, both *in vitro* and *in vivo*, have demonstrated that permethrin is active against both the adults and eggs of head lice. In clinical trials 1% permethrin was found to be an efficacious treatment for head lice. After one treatment over 98% of patients were free of head lice at 7 days and over 93% of patients were free of lice at 14 days, indicating that permethrin continues to exert activity after treatment. In the same study fewer than 2% of patients had viable eggs 7 days after a single application of 1% permethrin crème rinse and at 14 days less than 4% of patients had viable eggs.

STORAGE AND STABILITY

Kwellada-P Creme Rinse should be stored between 15° and 30°C.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Kwellada-P Creme Rinse is available in plastic bottles containing 50 mL and 200 mL crème rinse.

PART II: SCIENTIFIC INFORMATION

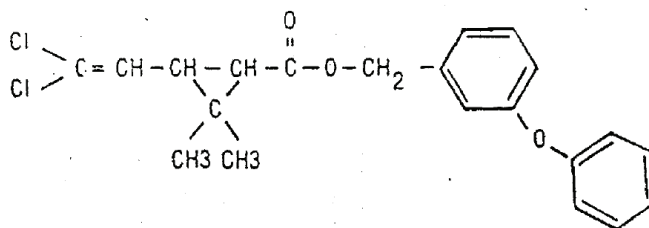
PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Permethrin

Chemical name: 3-phenoxybenzyl-(1R, 1S)-cis, Trans-3-(2, 2-dichloro vinyl)-2, 2-dimethylcyclopropanecarboxylate

Molecular formula and molecular mass: 391.29



Structural formula:

Physicochemical properties: a yellowish-brown viscous liquid

Solubility: insoluble in water, soluble in or miscible with most organic solvents (acetone, chloroform, cyclohexanone, ethanol, ether, hexane, methanol, dichloromethane, xylene)

Boiling Point: 198° - 200°C at 0.3 mm Hg

DETAILED PHARMACOLOGY

Clinical pharmacology studies demonstrated that 1% permethrin is efficacious when adult lice, nymphs and eggs are in contact with the permethrin for 10 minutes. In a small study of 20 heavily infected patient's treatment duration of 10 minutes was effective in killing 97.6% of lice within 2 hours. When the treatment was allowed to remain on the hair for 2 hours 100% of lice were dead 2 hours after treatment. The increased duration of treatment had no effect upon the hatch rate of eggs. Despite the presence of a few live lice on one patient 2 hours after a 10 minute treatment all patients were free of lice at a 7 day follow-up evaluation.

A pharmacology study demonstrated that when the amount of permethrin placed on the hair was decreased, the efficacy of the product decreased. In this study a standard single dose of 1% permethrin creme rinse was administered to 1, or 2 or 3 or 4 patients. Efficacy decreased with the decreasing amount of 1% permethrin creme rinse used. The diminished efficacy was particularly marked in females, probably due to the relative length of hair.

These studies confirmed that 10 minutes is an adequate application time and that the amount of permethrin applied is important for efficacy.

In a study of 9 healthy volunteers percutaneous absorption of permethrin from a single application of Kwellada-P Creme Rinse was insignificant and calculated to be less than 0.1% of the applied dose.

To demonstrate the efficacy of the Kwellada-P Creme Rinse, a single-centre, double-blind randomized, parallel study was conducted to compare its efficacy with NIX creme rinse. The study was conducted in a population where head lice infestations are common and pediculicides are rarely used and conducted in an environment where the temperature range was 26°C- 34°C. Since permethrin is more effective at lower temperatures, the study was conducted in conditions which were more adverse than conditions of use in Canada. There were no statistical differences between the treatment groups at baseline for demographic parameters. 119 patients were treated and completed the study.

The data showed that there were no significant differences at any time between Kwellada-P Creme Rinse and NIX for any of the parameters evaluated. Both products were efficacious with the pediculicidal rate at day 14 being 91.5% (54/59) for NIX and 90% (54/60) for Block 1% permethrin creme rinse. This study demonstrated that Kwellada-P Creme Rinse and NIX were comparable in efficacy.

TOXICOLOGY

Permethrin exists in both *cis*- and *trans*- forms. In insects both forms are comparable in their toxicity while in mammals the *cis*- isomer is more toxic than the *trans*- isomer. Acute toxicity studies demonstrated that while the *1R cis*- isomer had an LD₅₀ of about 96 mg/kg in mice when

administered orally, the LD₅₀ of the *1R trans*- isomer was 3,150 mg/kg and that of the *1S trans*- isomer was >5,000 mg/kg. The magnitude of difference in toxicity from insects to mammals is several hundred-fold with LD₅₀ values for both *cis*- and *trans*- isomers in the range of 0.09-0.6 mg/kg for such insects as cockroaches and adult houseflies.

Long-term studies of oral administration of permethrin determined that the no observed effect level in dogs treated for 6 months was 250 mg/kg.

Survival for rats and mice receiving up to 2,500 ppm for 104 and 98 weeks respectively was similar for treated and control groups. During the first 2 weeks there were slight tremors in the group of rats receiving 2,500 ppm. This side effect subsided with time. Hematological and clinical chemistry parameters were evaluated in the rat study and at 52 weeks there was a reduction in clotting factors in the 1,000 and 2,500 ppm but only a small decrease in the high dose males at the study end. There were no other changes in laboratory parameters which could be considered permethrin related. There were increases in the liver weights in the permethrin-treated animals but no other changes in organ weights. Liver hypertrophy was associated with the increased liver weights, microsomal enzyme activity and SER content of cells. These changes are considered to be an adaptive response of no toxicological significance.

There was no evidence of a carcinogenic effect in rats. There was no difference between controls and treated rats in the incidence of tumors. In male mice there was a slight increase in the incidence of pulmonary adenomas. However, there were no changes in the incidence of carcinoma of the lung in the mouse study or of any type of lung tumor in the rat. An additional factor in assessing carcinogenic potential is the fact that permethrin was shown to be negative in several mutagenicity assays.

Overall, there is little evidence of chronic toxicity with permethrin use.

REFERENCES

1. Casida JE, Gammon DW, Glickman AH and Lawrence LJ. Mechanisms of selective action of pyrethroid insecticides. *Ann Rev Pharmacol Toxicol* 1983; 23:413-438.
2. Hutson DH. The metabolic fate of pyrethroid insecticides in mammals. *Prog Drug Metab* 1979; 3: 215-252.

3. Ishmael **1** and Litchfield **MH**. Chronic Toxicity and Carcinogenic Evaluation of Permethrin in Rats and Mice. *Fundamental and Applied Toxicology* 1988; **11**: 308-322.
4. The bioavailability of permethrin following a single topical application of each of three pediculicidal products: permethrin creme rinse (1%), permethrin shampoo (1%) and NIX creme rinse (1%). Data on File. Block Drug Company (Canada) Ltd.
5. A randomized double-blind study to compare the safety and efficacy of permethrin R&C creme rinse (1%) vs. NIX permethrin creme rinse (1%) for the treatment of *Pediculosis Capitis*. Data on File. Block Drug Company (Canada) **Ltd.**

PART III: CONSUMER INFORMATION

Kwellada-P Crème Rinse
Permethrin Crème Rinse 1% (w/w)

This leaflet is part III of a three-part "Product Monograph" published when Kwellada-P Crème Rinse was approved for sale in Canada and is designed specifically for Consumers.

This leaflet is a summary and will not tell you everything about Kwellada-P Crème Rinse.

This leaflet is a guide with some important facts about the product. If you have any questions, please consult your doctor or pharmacist.

ABOUT THIS MEDICATION**For External Use Only****Keep out of Sight and Reach of Children**What the medication is used for:

Kwellada-P Crème Rinse is indicated for the treatment of head lice (*Pediculus Capitis*). It kills head lice and their nits (eggs) on contact.

What it does:**What are head lice?**

Head lice are tiny insects that live in human hair. They hatch from small eggs, called nits, which are attached to the base of individual hairs. The eggs hatch in about 7 to 10 days, with the new lice reaching maturity about 14 days later. The female louse can live for 20 to 30 days, and can lay as many as six eggs a day. Since lice multiply fast, they should be treated promptly.

Who suffers from head lice?

Getting head lice is not as bad as you think. It is not a sign of uncleanliness, or poor health habits. Head lice can occur at any age, and to either sex, so it is wise to learn how to recognize a head lice infestation and how to prevent it from coming back.

How does someone get head lice?

Head lice can be transmitted in a number of ways besides direct head to head contact. Borrowing a comb or brush from a person who has head lice will do it. So can bon-owing hats, ribbons, scarves or other head coverings. Sharing towels or pillows can also spread head lice. Even a stray hair that has nits can transmit head lice.

What signs should I look for?

Persistent itching of the back of the head and behind the ears can indicate head lice. You should also look for infected scratch marks or a rash on the scalp. Most important of all, look for nits attached to individual hairs at scalp level. These can be seen with the naked eye, but you can probably identify them more easily with the aid of a magnifying glass under strong light. Sometimes small white specks in the hair such as dandruff or droplets of hair spray can be confused with nits. Try removing the specks from the hair shaft. Dandruff or hair spray will come off easily- nits are very difficult to remove. Check with a health professional if you are not sure whether head lice are present.

Should other family members be checked?

Yes. If one member of your family has head lice, all household members and sexual partners should be checked and if necessary treated.

How can I prevent head lice in the future?

All family members should avoid borrowing personal items - combs, bmsbes, hats, towels or clothing - from each other or from friends. It is best for everyone to use his or her own personal articles, both at home and while away.

How to treat the environment?

All articles that may harbour lice or nits, such as clothes (worn 48 hours prior to treatment), towels and bed linens, should be washed in hot water, or dry cleaned or put in dryer hot setting 20 min or sealed in a plastic bag for 2 weeks then washed normally. For items that cannot be washed or dry cleaned eg. mattresses, upholstery, back seat of the car etc., use R&C II Spray insecticide. Combs and brushes should be disinfected by washing with pyrethrins, being careful to rinse thoroughly. Alternatively, combs and brushes can be disinfected by soaking in hot water (above 130°F or 54°C) for 5 to 10 minutes. Due to the contagious nature of head lice, it is advisable for all family members to be treated at the same time.

When it should not be used:

It is not to be used on individuals with known sensitivities or reactions to permethrin, any ingredients of the product, any synthetic pyrethroid or pyrethrin or to chrysanthemums.

It should not be used if you are pregnant, nursing, or planning to breastfeed.

Do not use in children under the age of two years.

What the medicinal ingredient is:

Permethrin 1% w/w as the active ingredient.

What the important non-medicinal ingredients are:

It also contains isopropyl alcohol, propylene glycol, stearalkonium chloride, lauryl alcohol, polyoxyethylene 4 lauryl ether, trolamine, polyquaternium-10 and Carbomer 980.

What dosage forms it comes in:

Kwellada-P Crème Rinse is available in plastic bottles containing 50 mL and 200 mL crème rinse.

WARNINGS AND PRECAUTIONS

What precautions should you take?

For external use only. Only use this product to treat existing headlice and nits. For best results use as directed- incorrect use may cause treatment failure. Avoid contact with eyes, nose, mouth and other mucous membranes as well as wounds and broken skin. This product may irritate your eyes. If applying routinely, wear gloves to avoid irritation. In case of contact, rinse with plenty of water. If skin irritation occurs, discontinue use and consult your doctor. If swallowed contact your doctor or Poison Control Centre immediately.

Keep out of sight and reach of children.

INTERACTIONS WITH THIS MEDICATION

No information available.

PROPER USE OF THIS MEDICATION

Usual dose:

How should you use Kwellada-P Crème Rinse?

1. Shampoo the hair with your regular shampoo, rinse with water and towel dry.
2. Shake Kwellada-P Crème Rinse well before using.
3. With scissors, snip off the tip of the enclosed applicator cap
4. Unscrew cap on bottle and replace with the applicator cap.
5. Apply Kwellada-P Crème Rinse to damp hair. Apply sufficient amount to saturate hair and scalp (25-50mL).
6. Leave on for 10 minutes.
7. Rinse thoroughly with water and dry with towel.
8. Remove dead lice and eggs with the following steps:

Comb wet hair with a regular comb to remove snarls; separate a strand of hair not wider than the nit comb. Using the enclosed nit comb tilted toward the scalp, comb the strand from scalp to end of hair repeat to remove all eggs, comb all strands in this manner.

9. Store unused product by removing the applicator cap from the bottle and replacing it with the original cap.
Store the product between 15°C- 30°C.
Rinse the applicator cap and air dry.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

When using Kwellada-P Crème Rinse you may experience: Tingling sensation in the limbs, skin irritation (including eczema, rash, swelling, reddening and itching) and skin discomfort (including smarting, a burning sensation and pain).

If any side effect should occur, discontinue use and contact your doctor.

OVERDOSE

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Symptoms and signs of overdose may include: Dizziness, loss of appetite, nausea, vomiting, headache, weakness, seizures, loss of consciousness.

HOW TO STORE IT

How should you store Kwellada-P Crème Rinse?
Store the product between 15-30°C

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at
www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - o Fax toll-free to 1-855-678-6789, or
 - o Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701C
Ottawa, ON K1A 0K9
- Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect/Health Canada Web site at
www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health care professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by: contacting the sponsor, Medtech Products Inc. at: 1-800-465-8811

This leaflet was prepared by Medtech Products Inc.

Last revised: June 26, 2012