

## PRODUCT MONOGRAPH

KWELLADA-P LOTION

Permethrin Lotion 5% w/w

Topical Scabicide

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## PRODUCT MONOGRAPH

### NAME OF DRUG

KWELLADA-P LOTION

Permethrin Lotion 5% w/w

### THERAPEUTIC CLASSIFICATION

Topical scabicide

### ACTIONS AND CLINICAL PHARMACOLOGY

Permethrin, a synthetic pyrethroid, has a broad spectrum of insecticidal activity combined with high potency when applied topically to insects.

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.

Clinical studies have demonstrated that permethrin is active against *Sarcoptes scabiei*, scabies. In clinical trials 5% permethrin was found to be an efficacious treatment for scabies. After one application of 5% permethrin lotion 93% of patients were cured at 28 days. At the interim assessment at 14 days 37% were already cured and 61% were improving.

Only a very minimal amount of permethrin is absorbed when applied topically. In a bioavailability study it was determined that <0.032% of a topically applied dose of 5% permethrin lotion was absorbed.

## INDICATIONS AND CLINICAL USE

Kwellada-P Lotion is indicated for the treatment of scabies *Sarcoptes scabiei*. One application of Kwellada-P Lotion is usually adequate to eradicate the infestation of scabies. If new lesions appear or live scabies mites are seen, a second treatment can occur seven to ten days after the initial treatment.

## CONTRAINDICATIONS

Kwellada-P Lotion is contraindicated in patients with a known sensitivity or reaction to permethrin, any components of the product, any pyrethroid, pyrethrin excipients, or to chrysanthemums.

## WARNINGS

Kwellada-P Lotion should be discontinued if hypersensitivity occurs. In the event of accidental ingestion of permethrin, please seek immediate medical attention.

## PRECAUTIONS

General: Permethrin is not an eye irritant, but contact with the eyes should be avoided because other components of the product may cause marked irritation. If this occurs, the eyes should be rinsed. During a scabies infestation the skin is often irritated resulting in erythema, edema and pruritus. These symptoms can be temporarily exacerbated after treatment with pruritus often persisting for several weeks after treatment. If skin irritation occurs and does not improve, consult a doctor. The treatment of eczematous-like reactions with corticosteroids should be withheld prior to treatment with permethrin, as there is a risk of exacerbating the scabies infestation by reducing the immune response to the mite. If applying routinely, wear gloves to avoid irritation. For best results use as directed – incorrect use may cause treatment failure.

Keep out of reach of children.

For external use only.

Use in Children: Kwellada-P Lotion is efficacious in children over 2 years of age. The safety and efficacy of Kwellada-P Lotion has not been established in children under the age of two months. For 2 years and up, use as directed. Do not use on children under 2 years of age. Long sleeve shirts, pants, mittens and socks should be worn on young children to prevent any contact of the treated skin with the mouth.

Use in the Elderly: Patients over 70 years should be treated under medical supervision.

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

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

## ADVERSE 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 burning, stinging and tingling were the most frequently reported adverse events with fewer than 1% of patients reporting them. The next most frequently reported event was pruritus followed by erythema which was reported by less than 0.02% of patients. Pruritus characteristically remains for several weeks after successful treatment. The itching gradually subsides with the natural loss of the upper layer of skin.

Other symptoms include paraesthesia, eczema, skin oedema, rash, skin irritation, skin discomfort, smarting, and pain of skin.

## SYMPTOMS AND TREATMENT OF OVERDOSAGE

There has been no incidence of ingestion of Kwellada-P Lotion. In the event of accidental ingestion of permethrin, please seek immediate medical attention.

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

For management of a suspected drug overdose, contact your regional Poison Control Centre.
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## DOSAGE AND ADMINISTRATION

Prior to application the skin should be clean, dry and cool. A hot bath should not be taken prior to treatment. The lotion should be thoroughly massaged into the skin from the neck to the soles of the feet, paying particular attention to the areas between the fingers and toes, under the fingernails and toenails, wrists, armpits, genital area and buttocks. Do not apply on head or face. Kwellada-P Lotion disappears when rubbed gently into the skin; therefore it is not necessary for the patient to apply the medication until it remains detectable on the skin. If the hands are washed with soap and water during the treatment period, Kwellada-P Lotion should be reapplied.

The patient should put on clean clothes and leave the lotion in place for 12 to 14 hours. The lotion should then be thoroughly washed off during a shower or bath. Patients should again change into clean clothes.

One treatment is usually adequate to eliminate the scabies. However, if live scabies mites are present or new skin lesions appear a second application can be given seven to ten days later.

Kwellada-P Lotion should be shaken before use.

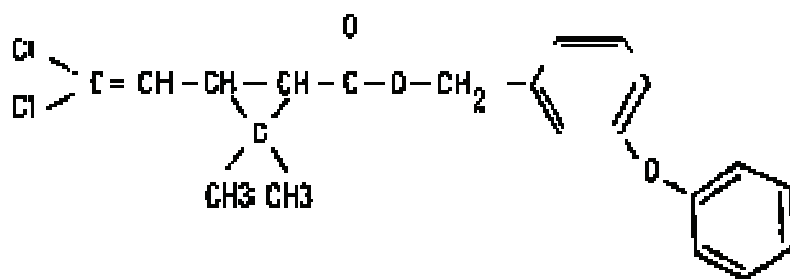
For External Use Only

## PHARMACEUTICAL INFORMATION

### 1. Drug Substance

Common Name: Permethrin

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



Molecular Weight: 391.29

Physical Form: 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

2. Composition

Kwellada-P Lotion contains permethrin cis/trans ratio of 25:75. It also contains carbomer 980, edetate sodium, imidurea, methylparaben, polysorbate 20, propylene glycol, propylparaben, purified water, sorbitan monolaurate and sodium hydroxide.

3. Stability and Storage Recommendations

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

AVAILABILITY OF DOSAGE FORMS

Kwellada-P Lotion is available in plastic bottles containing 100 mL lotion.

## INFORMATION FOR THE CONSUMER

Kwellada-P<sup>™</sup> Lotion  
Permethrin Lotion 5% (w/w)

Single treatment kills scabies mites and eggs in most cases.

**For External Use Only**  
**Keep out of Sight and Reach of Children**

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

### **What does Kwellada-P<sup>™</sup> Lotion contain?**

5% permethrin as the active ingredient.

### **When should you use Kwellada-P<sup>™</sup> Lotion?**

Kwellada-P<sup>™</sup> Lotion is indicated for the treatment of scabies (*Sarcoptes scabiei*). It kills scabies mites and eggs.

### **When should you not use Kwellada-P<sup>™</sup> Lotion?**

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.

If you are currently using a product to treat eczema, consult your physician before using Kwellada-P<sup>™</sup> Lotion. Stop treatment with steroids prior to using this product.

Use in Pregnancy: Do not use Kwellada-P Lotion if you are pregnant.

Use in Nursing Mothers: Because it is not known whether permethrin is excreted during lactation, consideration should be given to discontinuing nursing during treatment with Kwellada-P Lotion or withholding treatment if it is not possible to discontinue nursing.

Use in Children: For children 2 years and up, use as directed for adults. Long sleeve shirts, pants, mittens and socks should be worn on young children to prevent any contact of the treated skin with the mouth. Do not use on children under 2 years of age.

Use in the Elderly: If you are over 70 years of age, consult a health care professional before using this product.



**What precautions should you take?**

Do not use Kwellada-P<sup>™</sup> Lotion on the head or face. This product may irritate your eyes. In case of contact, rinse with plenty of water. Stop using if you experience skin irritation and consult a doctor if it doesn't improve. If swallowed contact your doctor or Poison Control Centre **immediately**. If a reaction occurs, discontinue use and consult your doctor. Avoid contact with eyes or the inside of mouth.

**Side effects and what to do about them?**

When using Kwellada-P<sup>™</sup> Lotion, 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).

Seek medical advice immediately if you swallow or take an overdose of Kwellada-P<sup>™</sup> Lotion. Symptoms and signs of overdose may include: Dizziness, loss of appetite, nausea, vomiting, headache, weakness, seizures, loss of consciousness.

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.

**How should you use Kwellada-P<sup>™</sup> Lotion?**

If applying routinely, wear gloves to avoid irritation. For best results use as directed – incorrect use may cause treatment failure.

**DIRECTIONS: SHAKE WELL**

1. Before applying Kwellada-P<sup>™</sup> Lotion, ensure that the skin is clean, dry and cool. Do not take a hot bath before treatment.
2. Thoroughly massage a sufficient quantity of the lotion into the skin to cover the entire area from the neck to the soles of the feet, paying particular attention to the areas between the fingers and toes, under the fingernails and toenails, wrists, armpits, genital area and buttocks.
3. Put on clean clothes.
4. Leave on for 12 to 14 hours. During the treatment period, if hands are washed, the lotion should be reapplied after washing.
5. Wash the entire body (shower or bath).

6. Change into clean clothes.
7. A second application may be given 7 to 10 days after the first treatment if live scabies mites are present or new skin lesions appear
8. All clothing, towels, bedding etc. should be washed in very hot water and by using the hot cycle in the dryer for at least 20 minutes. Dry cleaning should suffice for blankets, jackets and other non-washables. Mattresses which have been used by an infested person should not be used for 48 hours. Toilet seats, combs, etc. should be disinfected being careful to rinse thoroughly.

Note: Itching may last for several weeks following treatment with the drug.  
Retreatment is only necessary if live mites appear or new lesions develop.

The nature of Kwellada-P<sup>™</sup> Lotion is such that it disappears when rubbed gently into the skin. Therefore, it is not necessary to apply the lotion until it remains detectable on the surface.

Some itching may still persist for up to 2 weeks after treatment. This is due to the eggs and faecal pellets left behind by the mites in your skin. The itching will subside with the natural loss of the upper layer of skin.

A single application is usually sufficient but the procedure may be repeated 7 - 10 days later if new lesions develop.

Check all household members and treat them if necessary to prevent re-infestations.

### **How should you store Kwellada-P<sup>™</sup> Lotion?**

Store the product between 15-30°C

### **What is scabies?**

Scabies is a contagious infestation. The itching is the allergic response of the body to the mite. Just visible to the naked eye, the female mite burrows through the epidermal (upper) layer of the skin, leaving eggs and faecal pellets in the burrow behind her. It is proteins in the faecal material seeping into the tissue around the burrow which causes the body's reaction. The burrows can sometimes be detected, but are often scarce and difficult to find.

Like any allergy, it takes some time to become sensitized to the allergen and most people do not have any symptoms at all for 4-6 weeks after catching the infection. This means that there

is plenty of time to pass the disease on to others unknowingly!

### **Who suffers from scabies?**

Getting scabies is not as bad as you think; anyone can catch it. It is not a sign of uncleanliness, or poor health habits. The mite does not discriminate against age, sex, wealth, profession or race. So it is wise to learn how to recognize a scabies infection, and how to treat it successfully. Anyone with whom there is skin to skin contact could be a donor.

### **How does someone get scabies?**

Scabies is transmitted by skin to skin contact when the mites pass from person to person. This happens most frequently during that commonest of contacts - holding hands.

### **What signs should I look for?**

In people with normal immune systems (i.e. the majority of the general population) scabies produces classical symptoms. The most common is a widespread itchy rash which is particularly severe at night, or when the body is warm, e.g. after exercise or a warm bath. The classical scabies rash is widespread and can affect almost any part of the body. In adults it is absent from the centre of the chest and back and the head, but in infants the rash may be found in these places. In addition, you may also find skin lesions - wavy, threadlike, very small slightly elevated lesions between the fingers, on the elbows, hands and wrists. Other common sites of infestation are the stomach, thighs, genital area and buttocks.

### **Should other household members be treated?**

Yes. These infestations are spread by contact; all household members and sexual partners should be carefully examined and treatment instituted where necessary to prevent the spread of infestation.

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](http://www.healthcanada.gc.ca/medeffect)

Call toll-free at 1-866-234-2345

Complete a Canada Vigilance Reporting Form and:

Fax toll-free to 1-866-678-6789, or

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™ Canada Web site at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect).

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

## PHARMACOLOGY

A clinical trial was conducted in healthy volunteers to determine the bioavailability of permethrin following a single topical application of 5% permethrin lotion. The extent of permethrin absorption was assessed directly by determination of *cis*- and *trans*-permethrin in the blood and indirectly by determination of the major metabolites of permethrin (*cis*- and *trans*- dichlorovinyl acid) which are almost entirely excreted in the urine as free or conjugated forms.

The *cis*- and *trans*-permethrin levels were not detected in most plasma samples. When detected, *cis*-permethrin levels ranged from 6-96 ng/mL and *trans*-permethrin levels ranged from 8 to 15 ng/mL. When calculated using the highest detected levels, the maximum absorption was <0.032%.

To demonstrate the efficacy of Kwellada-P Lotion a single-centre, double-blind randomized, stratified, parallel study was conducted in scabies patients 2 years of age and older to compare its efficacy with NIX Dermal Cream. There were no statistically significant differences at baseline between the groups for any demographic variables. 114 patients were analyzed for safety and efficacy.

There was no significant difference in cure rates between the two products. Both products were efficacious for all age groups with the cure rate at day 28 being in excess of 92% for both products. This study demonstrated that Kwellada-P Lotion and NIX were comparable in efficacy. There were no adverse reactions reported in this study.

## 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 LD<sub>50</sub> of about 96 mg/kg in mice when administered orally, the LD<sub>50</sub> 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 LD<sub>50</sub> 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 nor 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 OR SELECTED BIBLIOGRAPHY

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3. Ishmael J and Litchfield MH. Chronic Toxicity and Carcinogenic Evaluation of Permethrin in Rats and Mice. *Fundamental and Applied Toxicology* 1988; 11: 308-322.
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5. A randomized double-blind study to compare the safety and efficacy of permethrin 5% lotion versus NIX Dermal Cream (5% permethrin) for the treatment of scabies. Data on File. Block Drug Company (Canada) Ltd.