For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

PERMITE

1. Generic Name

Permethrin Cream 5%

2. Qualitative and quantitative Composition:

Each g contains

Permethrin……..…..50 mg

Preservative

Formaldehyde Solution B.P……..0.1 % w/w

Cream base……....q.s

The Excipient used are Butylated Hydroxy Toluene, Carbomer, Coconut Oil, Cetomacrogol, Glyceryl Monostearate, Glycerin, Isopropyl Myristate, Lanolin Alcohol, Light Liquid Paraffin, Sodium Hydroxide.

3. Dosage form and strength

Dosage form: Cream

Strength: Permethrin (5%)

4. Clinical particulars

4.1 Therapeutic indication

It is indicated for the treatment of infestation with sarcopyto scabies.

4.2 Posology and method of administration

Adults and children

Thoroughly massage Permethrin Cream, 5% into the skin from the head to the soles of the feet. Scabies rarely infests the scalp of adults, although the hairline, neck, temple, and forehead may be infested in infants and geriatric patients. Usually 30 grams is sufficient for an average adult. The cream should be removed by washing (shower or bath) after 8 to 14 hours. Infants should be treated on the scalp, temple, and forehead.

One application is generally curative.

4.3 Contraindications

Permethrin Cream, 5% is contraindicated in patients with known hypersensitivity to any of its components, to any synthetic pyrethroid or pyrethrin.

4.4 Special warnings and precautions for use

If hypersensitivity to Permethrin Cream, 5% occurs, discontinue use.

General

Scabies infestation is often accompanied by pruritus, edema, and erythema. Treatment with Permethrin Cream, 5% may temporarily exacerbate these conditions.

Information for Patients

Patients with scabies should be advised that itching, mild burning and/or stinging may occur after application of Permethrin Cream, 5%. In clinical trials, approximately 75% of patients treated with permethrin cream, 5% who continued to manifest pruritus at 2 weeks had cessation by 4 weeks. If irritation persists, they should consult their physician. Permethrin Cream, 5% may be very mildly irritating to the eyes. Patients should be advised to avoid contact with eyes during application and to flush with water immediately if Permethrin Cream, 5% gets in the eyes.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Six carcinogenicity bioassays were evaluated with permethrin, three each in rats and mice. No tumorigenicity was seen in the rat studies. However, species-specific increases in pulmonary adenomas, a common benign tumor of mice of high spontaneous background incidence, were seen in the three mouse studies. In one of these studies there was an increased incidence of pulmonary alveolar-cell carcinomas and benign liver adenomas only in female mice when permethrin was given in their food at a concentration of 5000 ppm. Mutagenicity assays, which give useful correlative data for interpreting results from carcinogenicity bioassays in rodents, were negative. Permethrin showed no evidence of mutagenic potential in a battery of in vitro and in vivo genetic toxicity studies.

Permethrin did not have any adverse effect on reproductive function at a dose of 180 mg/kg/day orally in a three-generation rat study.

Pregnancy: Teratogenic Effects: Pregnancy Category B

Reproduction studies have been performed in mice, rats, and rabbits (200 to 400 mg/kg/day orally) and have revealed no evidence of impaired fertility or harm to the fetus due to permethrin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the evidence for tumorigenic potential of permethrin in animal studies, consideration should be given to discontinuing nursing temporarily or withholding the drug while the mother is nursing.

Pediatric Use

Permethrin Cream, 5% is safe and effective in pediatric patients two months of age and older. Safety and effectiveness in infants less than two months of age have not been established.

Geriatric Use

Clinical studies of permethrin cream, 5% did not identify sufficient numbers of subjects aged 65 and over to allow a definitive statement regarding whether elderly subjects respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. This drug is known to be substantially excreted by the kidney. However, since topical permethrin is metabolized in the liver and excreted in the urine as inactive metabolites, there does not appear to be an increased risk of toxic reactions in patients with impaired renal function when used as labeled.

4.5 Drugs interactions

No interactions are known.

The treatment of eczematous-like reactions with corticosteroids should be withheld prior to treatment with Permethrin 5% w/w Cream, as there is a risk of exacerbating the scabies infestation by reducing the immune response to the mite.

The likelihood of interactions between the two treatments leading to potentiated adverse reactions or reduced efficacy is, however, small.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are limited data on the use of Permethrin 5% w/w Cream in pregnancy which provide no indication of any risk to the foetus. Furthermore the amount of permethrin absorbed systemically following a whole body application is extremely low. Some permethrin may cross the placental barrier. The negative mutagenicity tests and the very low mammalian toxicity would suggest that any risk to the foetus following treatment with Permethrin 5% w/w Cream is minimal.

For precautionary reasons, the use of Permethrin 5% w/w Cream during pregnancy should be avoided unless physically acting treatment alternatives were ineffective and/or treatment with permethrin is required due to the woman's clinical condition.

Breast-feeding

Studies, following oral administration of permethrin in cattle have indicated that very low concentrations of permethrin are excreted in milk. It is not known whether permethrin is excreted in human breast milk. However, because only extremely small amounts of permethrin are absorbed systemically following treatment with Permethrin 5% w/w Cream and in theory only a very small percentage of this systemic permethrin may pass into the breast milk, it is unlikely that the concentrations of permethrin the milk will present any risk to the neonate/infant.

Fertility

Reproduction studies in mice, rats and rabbits given oral dosage of 200 to 400 mg/kg bodyweight/day revealed no evidence of impaired fertility. In addition permethrin did not show any adverse effects on the reproductive function of rats given an oral dosage of 180 mg/kg bodyweight/day in a three generation study.

There was no evidence of teratogenicity in reproduction studies in mice, rats and rabbits.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

In scabies patients, skin discomfort, usually described as burning, stinging or tingling, occurs in a few individuals soon after Permethrin 5% w/w Cream is applied. This occurs more frequently in patients with severe scabies and is usually mild and transient.

Other transient signs and symptoms of irritation, including erythema, oedema, eczema, rash and pruritus which may follow treatment of scabies with Permethrin 5% w/w Cream are generally considered to be part of the natural history of scabies.

In patients treated for scabies, itching may persist for up to 4 weeks post-treatment. This is generally regarded as due to an allergic reaction to the dead mites under the skin and is not necessarily indicative of a treatment failure**.**

System Organ Class	**Common(≥1/100 to<1/10)**	**Rare(≥1/10,000 to<1/1,000)**	**Very rare(<1/10,000)**	**Not known (cannot be estimated from the available data)**

Nervous system disorders	Paraesthesia, skin burning sensation	Headache		
Respiratory, thoracic and mediastinal disorders			Dyspnoea (in sensitive/allergic patients)	
Gastrointestinal disorders				Nausea
Skin and subcutaneous tissue disorders	Pruritus, erythematous rash, dry skin		Excoriation, folliculitis, skin hypopigmentation	Contact dermatitis, urticaria

Reporting of adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

No instance of accidental ingestion of Permethrin Cream, 5% has been reported. If ingested, gastric lavage and general supportive measures should be employed. Excessive topical use may result in increased irritation and erythema.

Symptoms of overdose may include nausea, headache, vomiting, dizziness and convulsion.

Application of a full tube of cream to a 2 month old would result in a dose of approximately 350 mg/kg bodyweight to skin. It is unlikely that such a dose would cause overt signs of systemic toxicity even if 100% of the permethrin were absorbed.

It is possible that excessive application of Permethrin 5% w/w Cream might result in localised adverse reactions or more severe skin reactions.

Symptomatic treatment is indicated should hypersensitivity-type reactions occur.

In the event of accidental ingestion of the contents of a tube of Permethrin 5% w/w Cream by a child, gastric lavage should be considered if consultation is within 2 hours of ingestion.

5 Pharmacological properties

5.1 Pharmacodynamic Properites

Permethrin, a pyrethroid, is active against a broad range of pests including lice, ticks, fleas, mites, and other arthropods. It acts on the nerve cell membrane to disrupt the sodium channel current by which the polarization of the membrane is regulated. Delayed repolarization and paralysis of the pests are the consequences of this disturbance. Permethrin is rapidly metabolized by ester hydrolysis to inactive metabolites which are excreted primarily in the urine. Although the amount of permethrin absorbed after a single application of the 5% cream has not been determined precisely, data from studies with ^{14}C-labeled permethrin and absorption studies of the cream applied to patients with moderate to severe scabies indicate it is 2% or less of the amount applied.

5.2 Pharmacokinetic properties

Investigations with the 5 % cream in humans revealed an average percutaneous absorption rate of 0.47 ± 0.3 % in healthy subjects and of 0.52 ± 0.3 % in patients.

Pharmacokinetic properties were studied in adult subjects only (6 healthy volunteers and 6 patients with scabies).

Absorbed permethrin is rapidly broken down by esterases as well as hydrolases. After oral administration, peak plasma concentrations are reached in approximately 4 hours. The isomeric mixture is then excreted in the urine in the form of glucuronides, sulfates etc as cis-trans CI2CA [(3- (2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid)] and after oxidation to 3 PBA (3- phenoxybenzoic acid). After oral application, up to 6 % is excreted unchanged in the faeces whilst on dermal application, unchanged permethrin is virtually undetectable.

6 Nonclinical properties

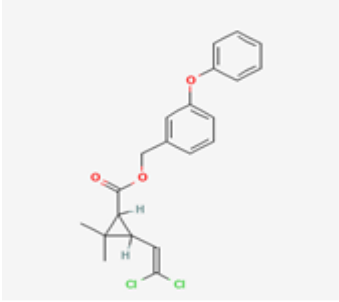
6.1 Animal Toxicology or Pharmacology

Six carcinogenicity bioassays were evaluated with permethrin, three each in rats and mice. No tumorigenicity was seen in the rat studies. However, species-specific increases in pulmonary adenomas, a common benign tumor of mice of high spontaneous background incidence, were seen in the three mouse studies. In one of these studies there was an increased incidence of pulmonary alveolar-cell carcinomas and benign liver adenomas only in female mice when permethrin was given in their food at a concentration of 5000 ppm. Mutagenicity assays, which give useful correlative data for interpreting results from carcinogenicity bioassays in rodents, were negative.

7 Description

Permethrin:

Permethrin is (3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane-1-carboxylate. The empirical formula is $C_{21}CL_2H_{20}O_3$ and its molecular weight is 391.3 g/mol. The structural formula is:



Permite:

Permethrin are a white smooth homogenous cream. The Excipient used are Butylated Hydroxy Toluene, Carbomer, Coconut Oil, Cetomacrogol, Glyceryl Monostearate, Glycerin, Isopropyl Myristate, Lanolin Alcohol, Light Liquid Paraffin, Sodium Hydroxide,

8 Pharmaceutical particulars

8.1 Incompatibilities

Not applicable

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

PERMITE is available in pack of 30 and 60 gm Cream.

8.4 Storage and handing instructions

Do not store above 30°C. Do not freeze.

Keep the tube tightly closed after use.

Avoid contact with eyes.

Keep out of reach of children.

To be used only under Medical Supervision.

9 Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10 Details of manufacturer

Encube Ethicals Pvt. Ltd

Plot No. C-1, Madkaim Industrial Estate,

Madkaim, Post Mardol, Ponda,

Goa – 403 404, India.

11 Details of permission or license number with date

Mfg. License No.: 361 Issued on: 20.06.1999

12 Date of revision

NA

MARKETED BY

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IN/Permite Cream 5%/Feb-24/01/PI