

SUMMARY PRODUCT CHARACTERISTIC (SPC)

Permethrin

5 % cream

1.1 Name of the medicinal product – Permethrin

1.2 International Non-property name – Permethrin

2. Qualitative and Quantitative Composition

Each gram contains:

active ingredient: permethrin – 50 mg;

For a full list of excipients, see section 6.1

3. Pharmaceutical form

White homogenous odorless cream.

4. Clinical particulars

4.1 Therapeutic indications

Permethrin cream is indicated for the treatment of scabies in adults and children >2 months of age, and crab lice in adults.

4.2 Posology and method of administration

Treatment of scabies

Adults and adolescents over 12 years of age:

Apply up to 30 g of cream (corresponding to 60% tube of 50 g).

Paediatric population

Children aged from 6 - 12 years:

Apply up to 15 g of cream (corresponding to 30% tube of 50 g).

Children aged from 2 months - 5 years:

Up to 7.5 g of cream (corresponding to 15% tube of 50 g).

The safety and efficacy of Permethrin cream in children under 2 months of age have not been established. No data are available.

Treatment of crab lice

Adults over 18 years of age:

Apply up to 30 g of cream (corresponding to 60% tube of 50 g).

Method of administration

For cutaneous use only. The medicinal product must not be swallowed.

Carefully apply a thin layer of cream to the skin (cutaneous use).

For treatment of scabies:

Adults should apply the cream uniformly to the whole body including the neck, palms of the hands and soles of the feet. The head and face can be spared unless scabies efflorescences are present in this region.

On application, the areas between the fingers and toes (also under the finger- and toe-nails), the wrists, elbows, armpits, external genitalia and the buttocks should be especially carefully treated.

Paediatric population

Children should apply the cream uniformly to the whole body, including the palms of the hands, soles of the feet, neck, face, ears, and scalp. Parts of the skin around the mouth (because the cream could be licked off) and the eyes should be spared. Children should be kept from licking the cream from the hands. If necessary, children should wear gloves.

Only limited experience is available with Permethrin cream in children aged 2 months to 23 months. Therefore treatment must be given only under close medical supervision in this age group.

Elderly:

Elderly patients (over 65 years) should use the cream in the same way as adults, but in addition, the face, ears and scalp should also be treated. Care should be taken to avoid applying the cream to areas of skin around the eyes.

Permethrin cream should be applied to clean, dry, cool skin. If the patient has taken a warm bath prior to treatment the skin should be allowed to cool before the cream is applied.

Permethrin cream is a vanishing cream and when rubbed gently into the skin it will disappear. Therefore, there is no need to continue to apply cream to the skin until it remains detectable on the surface.

Older children should be supervised by an adult when applying to ensure that a thorough treatment is administered.

The whole body should be washed thoroughly 8 – 12 hours after treatment.

Approximately 90% of individuals are cured with a single application of cream. If necessary, a second application may be given not less than 7 days after the initial application, if there are no signs of the original lesions healing or if new lesions are present.

For treatment of crab lice in adults:

Sufficient cream should be applied to cover the pubic region, perianal (around the anus), inner thighs down to the knees and any hair that grows up from the pubic area to the chest/stomach.

For treatment of crab lice in adults, the cream should be left on the skin for 24 hours, after which the treatment areas should be washed thoroughly.

Any facial hair (beards, moustaches) and eyelashes should be checked for the presence of live lice and eggs. Cream should be applied to any facial hair, carefully avoiding eyes. If live lice or eggs are found on the eyelashes they should be removed carefully using tweezers. Cream should not be applied to the eyelashes because the cream can cause moderate eye irritation.

4.3 Contraindications

Hypersensitivity to the active substance permethrin or other substances of the pyrethrin group or to any of the excipients listed in section 6.1. In such cases treatment should be switched to a chemically different antiscabies agent.

4.4 Special warnings and precautions for use

In the case of hypersensitivity to chrysanthemums or other compositae, treatment should only be given if strictly indicated. In such cases treatment should be switched to a chemically different agent.

When using Permethrin cream 5%, care should be taken not to allow the cream to get into the eyes or come into contact with mucous membranes (e.g. nasopharyngeal space, genital area) or open wounds.

Paediatric population

Only limited experience is available with Permethrin cream in children aged 2 months to 23 months. Therefore treatment must be given only under close medical supervision in this age group.

For cutaneous use only!

Permethrin cream 5% is harmful to all types of insects and also for aquatic forms of life (fishes, daphnia, algae). Contamination of aquaria and terraria is to be avoided.

Note: The excipients of the cream (liquid paraffin) can reduce the functioning and hence the reliability of latex products (e.g. condoms, diaphragms) used at the same time.

Cream contains cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).

Cream contains propylene glycol, which at threshold 50 mg/kg/day may cause skin irritation. Do not use this medicine in babies less than 4 weeks old with open wounds or large areas of broken or damaged skin (such as burns) without talking to your doctor or pharmacist.

Cream contains methylparaben, propylparaben, which may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction

No interactions are known.

The treatment of eczematous-like reactions with corticosteroids should be withheld prior to treatment with Permethrin 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 Fertility, pregnancy and lactation

There are limited data on the use of Permethrin 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 cream is minimal.

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 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 in the milk will present any risk to the neonate/infant.

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 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 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 ($\geq 1/100$ to $< 1/10$) | Rare ($\geq 1/10,000$ 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 suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via "Arpimed" LLC by going to www.arpimed.com and fill out the appropriate form "Report an adverse reaction or inefficiency of drug". Hotline number: (+374 55) 05 79 86. And by using "Centre of Drug and Medical Technology Expertise" SNPO, going to the site: www.pharm.am in "Report about adverse effect of medicine" section and fill out the "Report of adverse reaction or manufacturing problem of medicinal product". Hotline numbers: +37410200505; +37496220505.

4.9 Overdose

There are no reports of overdosage with Permethrin cream.

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 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 cream by a child, gastric lavage should be considered if consultation is within 2 hours of ingestion.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ectoparasiticides, incl. Scabicides. Pyrethrines, incl. synthetic compounds. Permethrin, combinations. **ATC CODE** - P03AC04.

The principal physiological action in insects (lice) exposed to permethrin is induction of electrochemical abnormalities across the membranes of excitable cells, leading to sensory hyperexcitability, incoordination and prostration. It is assumed that the mode of action against arachnids (mites) is similar.

Paediatric population

Newborns and infants:

The safety and efficacy of permethrin in newborns and infants under 2 months of age have not been established since no data are available from prospective trials or larger case series. A limited number of case reports in the treatment of children under 2 months of age presenting with scabies do not suggest specific safety concerns for the use of topical permethrin in this age group, but no definite conclusion can be drawn.

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.

5.3 Preclinical safety data

From acute and chronic toxicity studies there is no evidence indicating the occurrence of previously unknown adverse effects in humans. Furthermore there is no evidence on relevant genotoxic or carcinogenic potential. In studies on the reproductive toxicity in mice, rats and rabbits after repeated oral administration of permethrin effects were observed only for doses largely exceeding the

exposure expected for the topical use of the 5% cream. Following the intended use of this active substance a serious harmful effect on aquatic organisms (daphnia and fish) and terrestrial organisms (plants) is expected after passage of the sewage treatment plant.

6. Pharmaceutical particulars

6.1 List of excipients

Cetareth-12,
Cetareth-20,
Cetostearyl alcohol,
Liquid paraffin,
Propylene glycol,
Dimethicone,
Methylparaben,
Propylparaben,
Glycerol monostearate,
Water purified.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

Do not use this medicine after the expiry date.

6.4 Special precautions for storage

Store out of reach of children, in a dry place, protected from light at a temperature below 25⁰C.

6.5 Nature and contents of container

50 g of 5% cream for external use in an aluminum tube along with leaflet in the cardboard box.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorisation holder

“ARPIMED” LLC

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8. Date of first authorisation

12.11.2004

9. Date of revision of the text