Prescribing Information

1. NAME OF THE MEDICINAL PRODUCT

Polycutan

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Clotrimazole 1%
Neomycin sulfate 0.645%
Dexamethasone acetate 0.044%

Excipients with known effect:
Polycutan contains Cetostearyl alcohol and Benzyl alcohol.

For the full list of excipients, see Section 6.1

3. PHARMACEUTICAL FORM

Dermal white cream.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of dermatitis involving also a bacterial and/or fungal infection.

4.2 Posology and method of administration

Polycutan is for external topical use only.
Apply a thin layer of the cream twice daily (morning and evening) on the affected area and massage into the skin. If there is no improvement within a few days or if there is worsening, the condition should be assessed.

Elderly (over 65 years):
For Corticosteroids
Reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious using the least amount compatible with an effective therapeutic regimen and reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

Pediatrics
For Corticosteroids
Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced hypothalamic-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome than mature patients, because of a larger skin surface area to body weight ratio. Therefore, application of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

- Topical corticosteroids are contraindicated in tuberculosis of the skin, varicella and herpes simplex.

- The cream should not be applied in the external auditory canal of patients with perforated eardrum.

- Do not use the cream to treat scalp infections

4.4 Special warnings and precautions for use

- Polycutan is not intended for ophthalmic use.

- Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids. Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure, although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently. Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

- Ototoxicity and nephrotoxicity have been reported with the topical use of neomycin. This is especially important if the patient is also being concurrently treated with an aminoglycoside antibiotic. Therefore, caution is required when the preparation is prescribed for patients with aural or renal disease.

- When using neomycin-containing preparations to control secondary infection in chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitive to other substances, including neomycin.

For Corticosteroids

- If irritation, rectal bleeding or sensitization occurs, use should be discontinued. Prolonged use of corticosteroids may produce systemic effects.

- Systemic absorption of topical corticosteroids has produced reversible HPA axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients. Conditions which augment systemic absorption include the application of potent steroids, use over large surface areas, prolonged use, and the use of occlusive dressings, tight-fitting diapers and plastic pants. Such patients should be periodically evaluated for evidence of HPA axis suppression. This is performed using urinary-free cortisol and adrenocorticotropic hormone (ACTH) stimulation tests. If HPA axis suppression is noted, an attempt should be made either to reduce the frequency of application, or to substitute a less potent steroid. Recovery of the HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently,

signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids**.** If extensive areas are treated or if the occlusive technique is used, the possibility exists of increased systemic absorption and suitable precautions will be required in patients with electrolyte imbalance, gastrointestinal disturbances, diabetes, myopathy, cataract, renal or hepatic impairment, osteoporosis, and hemorrhage.

- Systemic corticosteroids have also been implicated in the development, reactivation perforation and delayed healing of peptic ulcers.

- In the presence of renal disease with a fixed or decreased glomerular filtration rate, systemic corticosteroids may cause edema.

- Adrenocorticosteroids may promote progression of cataracts especially with the use of high- to very high-potency products in periorbital area. Adrenocorticosteroids may cause an increase in the intraocular pressure especially with the use of high- to very high-potency products in periorbial area.

- If a local infection is already present at the area of treatment an appropriate antimicrobial agent should be used concurrently since corticosteroids may cause an exacerbation of the infection while the local anesthetic effect may be decreased due to an alteration in the pH of the anesthetic agent by the local infection at the treatment site.

- Corticosteroids may influence the immune system therefore caution should be exercised upon administration of these agents.

General
- If sensitization or irritation occurs, medication should be discontinued. If the sensitivity is attributed to the antibiotic component, neomycin-containing products should be avoided by the patient in the future.

- If local infection should continue or become severe, or in the presence of systemic infection, appropriate antimicrobial therapy should be instituted. If a favorable response is not obtained, this medication should be discontinued temporarily, until the infection has been controlled.

- As with other antibiotic-containing preparations, prolonged use may result in overgrowth of non-susceptible organisms including fungi. Appropriate measures should be taken if this occurs. When using neomycin-containing products to control secondary infection in chronic dermatoses, such as chronic otitis externa or stasis dermatitis, it should be borne in mind that the skin is more liable to become sensitive to other substances, including neomycin.

- Because of the concern of possible nephrotoxicity and ototoxicity associated with neomycin, this preparation should not be used over a wide area or for extended periods of time.

- Application of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen (see Use in Pediatrics).

- *Laboratory Tests*
The urinary free cortisol test and the ACTH stimulation test may be helpful in evaluating the HPA axis suppression. Systemic effects of excessive levels of the cortisone component may include a reduction in the number of circulating eosinophils and a decrease in urinary excretion of 17-hydroxycorticosteroids.

- *Excipient with known effect*

This product contains Cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis). The cream also contains Benzyl alcohol which may cause allergic reactions and mild local irritation.

4.5 Interaction with other medicinal products and other forms of interaction

- Following significant systemic absorption, neomycin can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents. However, the neuromuscular blocking activity of neomycin sulfate is unlikely to present a hazard during use of this preparation.

- Laboratory tests have suggested that, when used together, this product may cause damage to latex contraceptives. Consequently, the effectiveness of such contraceptives may be reduced. Patients should be advised to use alternative precautions for at least five days after using this product.

4.6 Fertility, Pregnancy and lactation

Fertility:

Clotrimazole
No human studies of the effects of clotrimazole on fertility have been performed; however, animal studies have not demonstrated any effects of the drug on fertility.

Neomycin sulfate and Dexamethasone acetate
No data available.

Pregnancy:

Clotrimazole
There is a limited amount of data from the use of clotrimazole in pregnant women. Animal studies with clotrimazole have shown reproductive toxicity at high oral doses (see section 5.3). At the low systemic exposures of clotrimazole following topical treatment, harmful effects with respect to reproductive toxicity are not predicted. Clotrimazole can be used during pregnancy, but only under the supervision of a physician.

Dexamethasone acetate
There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the embryo or fetus. Infants born to mothers who have been treated with large amounts of corticosteroids during pregnancy, or for prolonged periods of time, should be observed carefully for signs of hypoadrenalism.

Neomycin sulfate
No data available.

Lactation:

Clotrimazole
There are no data on the excretion of clotrimazole into human milk. However, systemic absorption is minimal after administration and is unlikely to lead to systemic effects. Clotrimazole may be used during lactation.

Neomycin sulfate and Dexamethasone acetate

It is not known whether topical administration of corticosteroids can result in sufficient systemic absorption to produce detectable quantities in breast milk. Nevertheless, caution should be exercised when topical corticosteroids are applied to nursing mothers.
There is little information to demonstrate the possible effect of topically applied neomycin in lactation.

4.7 Effects on ability to drive and use machinery

Clotrimazole
Clotrimazole has no or negligible influence on the ability to drive or use machines.

Neomycin sulfate and Dexamethasone acetate
No data available.

4.8 Undesirable effects

As the listed undesirable effects are based on spontaneous reports, assigning an accurate frequency of occurrence for each is not possible.

Immune system disorders: anaphylactic reaction, angioedema, hypersensitivity.

Vascular disorders: syncope, hypotension.

Respiratory, thoracic and mediastinal disorders: dyspnoea.

Skin and subcutaneous tissue disorders: blisters, contact dermatitis, erythema, paraesthesia, skin exfoliation, pruritus, rash, urticaria, stinging/burning sensation of the skin.

General disorders and administration site conditions: application site irritation, application site reaction, oedema, pain.

Corticosteroids
The following local adverse reactions have been reported infrequently with topical corticosteroids: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae and miliaria.

A wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood, and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations, and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances, and cognitive dysfunction including confusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown.

General
Allergic cross-reactions may occur which could prevent the future use of any or all of the following antibiotics for the treatment of infections: kanamycin, paromomycin, streptomycin, gentamicin. Signs of a sensitivity reaction to neomycin may appear, usually in the form of a low-grade reddening with swelling, dry scaling and itching, or simply as a failure to heal. However, signs of sensitivity reactions to neomycin may appear. During long-term use of neomycin- containing preparation, periodic examination for such signs is recommended. If they occur, patients should be advised to discontinue treatment.

It should be noted that these adverse reactions may occur more frequently with occlusive dressings, tightfitting diapers or plastic pants.

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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il
In additionally, you can report to Padagis via the following address: padagis.co.il

4.9 Overdose

Clotrimazole
No risk of acute intoxication is seen as it is unlikely to occur following a single dermal application of an overdose (application over a large area under conditions favourable to absorption) or inadvertent oral ingestion. There is no specific antidote.

However, in the event of accidental oral ingestion, gastric lavage is rarely required and should be considered only if a life-threatening amount of Clotrimazole has been ingested within the preceding hour or if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). Gastric lavage should be carried out only if the airway can be protected adequately.

Neomycin sulfate and Dexamethasone acetate
No data available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Clotrimazole
Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the fungal cytoplasmic membrane. Clotrimazole has a broad antimycotic spectrum of action in vitro and in vivo, which includes dermatophytes, yeasts, moulds, etc.
Under appropriate test conditions, the MIC values for these types of fungi are in the region of less than 0.062-8.0 µg/ml substrate. The mode of action of clotrimazole is primarily fungistatic or fungicidal depending on the concentration of clotrimazole at the site of infection. In vitro activity is limited to proliferating fungal elements; fungal spores are only slightly sensitive.
In addition to its antimycotic action, clotrimazole also acts on gram-positive microorganisms (Streptococci / Staphylococci / Gardnerella vaginalis), and gram- negative microorganisms (Bacteroides).
In vitro clotrimazole inhibits the multiplication of Corynebacteria and gram-positive cocci - with the exception of Enterococci - in concentrations of 0.5-10 µg/ml substrate.
Primarily resistant variants of sensitive fungal species are very rare; the development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.

Neomycin sulfate
Broad-spectrum antibiotic.

Dexamethasone acetate
Anti-inflammatory and anti-allergic glucocorticoid.

5.2 Pharmacokinetic properties

Clotrimazole
Pharmacokinetic investigations after dermal application have shown that clotrimazole is minimally absorbed from the intact or inflamed skin into the human blood circulation. The resulting peak serum concentrations of clotrimazole were below the detection limit of 0.001 mcg/ml, suggesting that clotrimazole applied topically is unlikely to lead to measurable systemic effects or side effects.

Neomycin sulfate and Dexamethasone acetate
No data available.

5.3 Preclinical safety data

Clotrimazole
Non-clinical data reveal no special hazard for humans based on studies of repeated dose toxicity, genotoxicity and carcinogenicity. Clotrimazole was not teratogenic in reproductive toxicity studies in mice, rats and rabbits. In rats high oral doses were associated with maternal toxicity, embryotoxicity, reduced foetal weights and decreased pup survival. In rats clotrimazole and/or its metabolites were secreted into milk at levels higher than in plasma by a factor of 10 to 20 at 4 hrs after administration, followed by a decline to a factor of 0.4 by 24 hrs.

Neomycin sulfate and Dexamethasone acetate
No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

2-Octyldodecanol
Cetostearyl alcohol
Cetyl Esters wax
Sorbitan monostearate
Polysorbate 60
Benzyl alcohol
Purified water

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

After first opening: 6 months.

6.4 Special precautions for storage

Store in a cool place below 25°C.

6.5 Nature and contents of container

Polycutan is available in 15 g or 30 gr Aluminium tubes with polyethylene caps.

7 Manufacturer and Registration Holder

Padagis Israel Agencies, 1 Rakefet St., Shoham, Israel

8 Registration Number

048-52-23172

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