SUMMARY PRODUCT CHARACTERISTIC (SPC)

1. NAME OF THE MEDICINAL PRODUCT
Dermatril, cream for topical use

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each gram of DERMATRIL cream contains:
active ingredients: betamethasone [as dipropionate] - 0.5 mg(0.65mg), clotrimazole - 10 mg, gentamicin sulfate - 1 mg;
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
White, odorless cream.

4. CLINICAL PARTICULARS.
4.1. Therapeutic indications
Dermatril is indicated for the treatment of corticosteroid-responsive dermatoses when complicated by infections caused by bacteria and/or fungi or when the possibility of such infections is suspected. The cream is suitable for the use of oozing lesions.

4.2 Posology and method of administration.
Adolescents and adults.
2 times a day (in the morning and in the evening) apply a thin layer on the affected areas of the skin and rub easily, and it is necessary to cover both the entire affected area and the surrounding healthy skin surface.
Duration of therapy varies depending upon the results of clinical examination, microbiological testing and patient response to treatment.
In the case of foot mycoses a longer course of treatment (2-4 weeks) should be considered.
Children 2 to 12 years old.
A small amounts apply on affected skin areas only and massage gently. Use no more than twice in a day with an interval at least 6-12 hours.
Under the care of a physician only the cream should be applied to face, neck, scalp, genital area, rectal area and intertrigo. Duration of treatment is limited to 5-7 days.
See also sections “Precautions” and "Use in children".

4.3. Contraindications.
Topical corticosteroids are contraindicated in skin infections (viral, bacterial [including tuberculosis] and fungal origin), reaction to vaccines, skin ulcers and acne. Cream should not be applied for face in the case of rosacea or perioral dermatitis.
Hypersensitivity to any of active components or ingredients of the preparation, other aminoglycosides (polyvalent allergy to gentamycin) or imidazole derives (polyvalent allergy to clotrimazole).
Dermatril is not indicated for use with occlusive dressing.
Dermatril should not be applied on mucosae, skin around eyes and close to eyes.

4.4. Special warnings and precautions for use
If irritation or sensitization develops with the use of Dermatril treatment should be discontinued and appropriate treatment instituted.
The systemic absorption of active ingredients for topical use may be increased if extensive body surface areas are treated with Dermatril especially for prolonged periods or on the injured skin.

At such circumstances, any of the side effects that have been reported following systemic use may also occur with topical use. Suitable precautions should be taken in these circumstances, particularly with children.
A cumulative toxic effect should be expected (ototoxicity, nephrotoxicity) due to increased transcutaneous absorption when aminoglycosides for systemic use are co-administrated.
The probability of polyvalent allergy to other aminoglycosides should be taken into account.
Prolonged use of antibiotic-containing preparations could result in growth of insensitive microorganisms. In such case or if a superinfection is developed the appropriative treatment should be started. Extensive use and the use of occlusive dressings of high-dose potent or very potent corticosteroid should be monitored closely by physician, especially taking into account the suppression of endogenous corticosteroids and possibility of metabolic effect.
Use on an open wound and damaged skin should be avoided.
Continuous use during 2 to 3 weeks should not be exceed, if possible.
If used very potent, potent and moderate corticosteroids on the face or genital areas, the special care should be taken and courses should be limited to 1 week.
On the areas around eyes only mild corticosteroids should be used (due to the risk of glaucoma).
Corticosteroids might mask symptoms of allergic skin reaction to ingredients of the drug.
The preparation contains propylene glycol and cetostearyl alcohol as excipients. When used externally, propylene glycol may cause skin irritation, and alcohol cetostearyl - skin reactions (eg, contact dermatitis).
Patient should be informed to use the drug for current skin disease only and do not share the drug with other people.
Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.
Use in children.
This preparation is not recommended for children under 2 years.
Pediatric patients may demonstrate greater susceptibility to topical corticosteroidinducedhypothalamic- pituitary-adrenal (HPA) axis suppression and to exogenous corticosteroid effects than mature patients because of greater absorption due to a large skin surface area to body weight ratio.
HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids.
Manifestations of adrenal suppression in children include low plasma cortisol levels and absence of response to ACTH stimulation. Manifestations of intra-cranial hypertension include a bulging fontanelle, headaches and bilateral papilledema.

4.5 Interaction with other medicinal products and other forms of interaction
If Dermatril to be applied on the skin of genital or anal area, such excipients as liquid paraffin, at simultaneous use of condoms from latex, it can lead to reduction of durability of condoms by a gap, and, therefore, to fail of their reliability.
Topical clotrimazole can demonstrate antagonistic action with respect to amphotericin and other polyene antibiotics.

4.6. Fertility, pregnancy and lactation
Pregnancy.
Studies in animals have shown teratogenic action of topical corticosteroids. There are no data in pregnant women.

Aminoglycosides cross the placenta and can be harmful to the foetus if woman use aminoglycosides during pregnancy.
Complete, irreversible, bilateral congenital deafness have reported in children from women who used aminoglycosides, including gentamycin, during pregnancy.
Data on topical use of gentamycin in pregnancy are not sufficient.
Data on use of clotrimazole in pregnancy are not sufficient.
Studies in animals have shown no evidence of risks for the foetus.
Dermatril should be use only if clearly necessary.
Dermatril should not be applied to a large surface area, in large amounts or during long time.
Nursing Women.
It is not known whether gentamycin, clotrimazole or corticosteroids for topical use are secreted in human milk. However, corticosteroids which appear in the blood, are also secreted in human milk. Breast feeding is contraindicated when Dermatril is to be applied on breasts.

4.7 Effects on ability to drive and use machines
Generally, the drug has no effects on ability to drive and use machines.

4.8. Undesirable effects
At the beginning of treatment.
Skin.
Rare: irritation, burning, itching, dry skin, hypersensitivity to any component of the drug, skin discoloration.
When used for large skin area, with occlusive dressing and/or prolonged use.
Local skin disorders are possible if extensive body surface areas are treated, if the occlusive technique is used or if treatment is prolonged. Systemic effect (adrenal suppression) is probable if extensive body surface areas are treated. Due to decreased local resistance to infections there is increased risk for secondary infection.
Skin.
Local skin disorders such as atrophy (especially on the face), telangiectasia, striae, strip-like skin atrophy, skin haemorrhagy, purpura, steroid acne, rosacea-like or perioral dermatitis, hypertrichosis, skin discoloration. Not known if the skin discoloration is reversible.
Uncommon: contact sensitivity to gentamycin.
Some patients have experienced the evident photosensitivity which, however, did not recur after repeated using gentamycin with the subsequent influence of UV-radiation.
Endocrine system.
Suppression of endogenous corticosteroids synthesis, hypercorticalism with oedema.
Nutrition disorders.
Diabetes mellitus (manifestation of latent form).
Ear, labyrinth / renal disorders
During treatment with using cream on extensive skin areas or applications on the injured skin when administered concurrently with systemic aminoglycosides, the cumulative ototoxicity/nephrotoxicity can occur.
Musculoskeletal disorders.
Osteoporosis, growth retardation (children).
Systemic adverse reactions, such as vision blurred, have also been reported with the use of topical corticosteroids.
In case of appearance the listed adverse reactions, and also the reactions which are not listed in this instruction for medical use of the drug, it is necessary to address to the doctor.
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 Scientific Centre of Drug and Medical Technology Expertise after academician E. Gabrielyan ″CJSC ″, 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
Symptoms: pituitary-adrenal axis suppression with development of secondary adrenal insufficiency and manifestations of hypercorticalism symptoms, including Cushing's syndrome is possible with prolonged usage or if extensive body surface areas are treated.
Such symptoms should not be considered as gentamycin overdose. Overgrowth of insensitive microorganisms is possible with prolonged usage of gentamycin or if extensive body surface areas are treated.
Using clotrimazole with occlusive dressings during 6 hours did not resulted to manifestations of overdose symptoms.
Treatment: appropriate symptomatic treatment is indicated. Acute hypercorticoid symptoms are virtually reversible. Treat electrolyte imbalance, if necessary. In cases of chronic toxicity, slow withdrawal of corticosteroids is advised. If overgrowth of resistant microorganisms occurs, Dermatril should be withdraw and appropriate treatment instituted.

5. PHARMACOLOGICAL PROPERTIES
Mechanism of Action Dermatril combines the following:
anti-inflammatory action of betamethasone dipropionate, antibiotic activity of gentamicin and antifungal activity of clotrimazole.

5.1. Pharmacodynamic properties:
ATC code: D07XC01
Betamethasone dipropionate is potent corticosteroid (class 3) with anti-inflammatory, antiallergic and antipruritic actions.
Gentamicin is aminoglycoside antibiotic with antibacterial action. The drug inhibits protein synthesis in susceptible bacteria. Gentamicin is active against many aerobic gram-negative bacteria and some aerobic gram-positive bacteria. In vitro, gentamicin concentrations of 1-8 μg/ml inhibit most susceptible strains of *Escherichia coli, Haemophilus influenzae, Moraxella lacunata, Neisseria,* indole positive and indole negative *Proteus, Pseudomonas* (including most strains of Ps. aeruginosa), *Staphylococcus aureus, S. epidermidis,* and *Serratia.* However, different species and different strains of the same species may exhibit wide variations in susceptibility in vitro. In addition, in vitro susceptibility does not always correlate with in vivo activity. Gentamicin is inactive against fungi, viruses, and most anaerobic bacteria.
Gentamicin is only minimally active against *Streptococci.*
Resistance to gentamicin has been demonstrated in both gram-negative and gram-positive bacteria.
Clotrimazole is a synthetic imidazole derivative with antifungal activity. Active against fungi which are pathogenic for both humans and animals. Clotrimazole is effective against dermatophytes, yeasts and
molds. In vitro, clotrimazole exhibits fungistatic and fungicidal activity against isolates of *Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, Microsporum canis* and *Candida species* including *Candida albicans.* Clotrimazole acts against fungi by inhibiting ergosterol synthesis.
Ergosterol is an important constituent of fungal membranes.

5.2. Pharmacokinetic properties
There are no data on pharmacokinetic properties of Dermatril
Betamethasone.
Under normal conditions only portion of betamethasone appears in the blood after topical use. The extent of penetration and absorption is determined by the skin area, the integrity of the skin, the pharmaceutical form used, age and method of application.
Gentamicin.
The transcutaneous absorption is not expected if gentamicin is applied on intact skin. If gentamicin is applied on skin that has lost the keratin layer of inflamed skin, used with occlusive dressing or on extended areas, the increased transcutaneous absorption should be expected.
Clotrimazole.
Greater amount of applied clotrimazole remains in the stratum corneum; absorption into blood is minor. Six hours after the application of radioactive clotrimazole 1% onto intact and acutely inflamed skin, the concentration of clotrimazole was following: 100 mcg/cm3 in the stratum corneum, 0.5 to 1 mcg/cm3 in the stratum reticulare, 0.1 mcg/cm3 in the subcutis.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Ceteareth-12
Ceteareth-20
Cetostearyl alcohol
Liquid paraffin
Propylene glycol
Dimethicone
Methylparaben
Propylparaben
Ethanol 96%
Water purified.

6.2. Incompatibilities
Not applicable.

6.3. Shelf life
3 years.
Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

6.4 Special precautions for storage
Store at a room temperature (15-25°C), in a dry place, out of the reach of children. Protect from light.

6.5 Nature and contents of container
15 g of cream is filled into aluminum tubes which are packed and inserted with the leaflet into cardboard boxes.

6.6 Special precautions for disposal and other handling
No special requirements.

7. Marketing authorization holder
"ARPIMED" LLC
Republic of Armenia, Kotayki Marz, Abovyan, 2204, 2nd Micro-District,19 Building
Tel.: (374) 222 21703 Fax: (374) 222 21924

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorization
06.11.2007 (Date of first authorisation)

10. **Date of revision of the text**