MERCK

Gentacortin®

Fluprednidene–21–Acetate + Gentamicin Sulfate

Specific skin corticosteroid cream with antibiotic

1. QUALITATIVE AND QUANTITATIVE COMPOSITION
Gentacortin cream contains Fluprednidene-21-acetate 0.1% and Gentamicin sulfate equivalent to Gentamicin 0.1% in a well-tolerated special cream base.

2. PHARMACEUTICAL FORM
Cream.

3. CLINICAL PARTICULARS
3.1 Indications
Gentacortin is indicate in the following skin diseases, particularly where bacterial infections are present or suspected:
- Eczema vulgaris (dermatitis) of all aetiology, phases and forms;
- Dyshidrotic eczema; Seborrhoic dermatitis;
- Lichen planus;
- Atopic dermatitis (endogenous eczema, neurodermatitis disseminata);
- Insect bites and stings;
- Dermatitis solaris (sunburn);
- Small first and second degree burns and chemical burns; and especially under occlusive dressing,
- Psoriasis vulgaris and
- Lichen simplex chronicus (neurodermatitis circumscripta).

Tolerance
Gentacortin is exceptionally well tolerated.

3.2 Posology and Method of Administration
Gentacortin cream should be applied gently to the lesion 3 or 4 times daily. The area treated may be covered with a gauze dressing if desired. In impetigo contagiosa, the crusts should be removed before application of gentamicin to permit maximum contact between the antibiotics and infection.

Duration of administration
Gentacortin cream should be applied to the affected parts of the skin for as there is a bacterial finding.

3.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients.

The following conditions should not be treated with Fluprednidene-21-acetate:
- Unresolved cutaneous viral, bacterial or fungal infections
- Rosacea
- Acne vulgaris
- Pruritus without inflammation
- Perianal and genital pruritus
- Perioral dermatitis
- Widespread plaque psoriasis, except single lesions
- Varicella
- Cases of smallpox
- Vaccination reaction
- Skin tuberculosis and syphilis

3.4 Special Warnings and Special Precautions for Use
Gentacortin should be used with caution in patients with a history of local hypersensitivity to corticosteroids or to any of the excipients in the preparation. Local hypersensitivity reactions *(see section Undesirable effects)* may be resemble symptoms of the condition under treatment.

Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, leading to glucocorticosteroid insufficiency, can occur in some individuals as a result of increased systemic absorption of topical steroids. If either of the above are observed, withdraw the drug gradually by reducing the frequency of application, or by substituting a less potent corticosteroid. Abrupt withdrawal of treatment may result in glucocorticosteroid insufficiency *(see section Undesirable effects)*. The risk with topical corticosteroids is reduced but potentially still exists.

Risk factors for increased systemic effects are:
- Potency and formulation of topical steroid
- Duration of exposure
- Application to a large surface area
- Use on occluded areas of skin (e.g. on intertriginous areas or under occlusive dressings (in infants the nappy may act as an occlusive dressing))
- Increasing hydration of the stratum corneum
- Use on thin skin areas such as the face
- Use on broken skin or other conditions where the skin barrier may be impaired
- In comparison with adults, children and infants may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic adverse effects. This is because children have an immature skin barrier and a greater surface area to body weight ratio compared with adults.

Visual disturbance
Visual disturbance may be reported with systemic and topical 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 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.

Children
In infants and children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression can occur.

Children are more susceptible to develop atrophic changes with the use of topical corticosteroids. If Fluprednidene-21-acetate is required for use in children, it is recommended that the treatment should be limited to only a few days and reviewed weekly. Occlusion should not be used.

Infection risk with occlusion
Bacterial infection is encouraged by the warm, moist conditions within skin folds or caused by occlusive dressings. When using occlusive dressings, the skin should be cleansed before a fresh dressing is applied.

Prolonged use of uninterrupted occlusion or use with extensive occlusive dressing may suppress adrenocortical function.

Use in Psoriasis
Topical corticosteroids should be used with caution in psoriasis as rebound relapses, development of tolerance, risk of generalized pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin have been reported in some cases. If used in psoriasis careful patient supervision is important.

Application to the eyelids
If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as cataract and glaucoma might result from repeated exposure.

Concomitant infection
Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and administration of appropriate antimicrobial therapy.

Application to the face
Application to the face is undesirable as this area is more susceptible to atrophic changes. If used on the face, treatment should be limited to only 5 days.

There have been a few reports in the literature of the development of cataracts in patients who have been using corticosteroids for prolonged periods of time. Although it is not possible to rule out systemic corticosteroids as a known factor, prescribers should be aware of the possible role of corticosteroids in cataract development.

Chronic leg ulcers
Topical corticosteroids are sometimes used to treat the dermatitis around chronic leg ulcers. However, this use may be associated with a higher occurrence of local hypersensitivity reactions and an increased risk of local infection.

Fluprednidene–21–acetate associated with Gentamicin sulfate
Gentacortin is not recommended to be applied to the ear. Gentamicin in Gentacortin may cause topically induced ototoxicity.

Gentacortin cream is not intended for use on the eye and mucous membranes.

The possibility of nephrotoxicity and/or neurotoxicity due to absorption of topical application should be kept in mind. Similarly, cross-tolerance and cross-allergenicity occurring with corticosteroids and aminoglicosides should be born in mind. Overgrowth of non-susceptible organisms, including fungi, occasionally occurs with topical antibiotics including Gentamicin. If this occurs, or if irritation, sensitization or superinfection develops, treatment with Fluprednidene-21-acetate associated with Gentamicin sulfate should be discontinued.

In patients requiring systemic (oral, i.m., i.v., etc.) and local antibiotic therapy, priority should be given to systemic treatment. In this case local treatment should not be carried out with the same antibiotic to avoid resistance development. Use of topical Gentamicin occasionally allows overgrowth of non-susceptible organisms, including fungi. If this occurs, or if irritation, sensitization or superinfection develops, treatment with Gentamicin should be discontinued and appropriate therapy instituted.

Continuous and routine use in hospitalization is not recommended as it may cause resistance.

3.5 Interaction with Other Medicinal Products and Other Forms of Interaction
Co-administered drugs that can inhibit CYP3A4 (e.g. Ritonavir and Itraconazole) have been shown to inhibit the metabolism of corticosteroids leading to increased systemic exposure. The extent to which this interaction is clinically relevant depends on the dose and route of administration of the corticosteroids and the potency of the CYP3A4 inhibitor.

3.6 Fertility, Pregnancy, and Lactation
Fertility
There are no data in humans to evaluate the effect of topical corticosteroids on fertility.

SPECIFICATION

Material name	: Gentacortin Insert
Article No	: 10470505356V02
Dimension	: 200 x 145 mm
Material Quality	: HVS 60 gsm
Varnish & Finishing	: -
Barcode No.	: -
Pharmacode No.	: -
Color	: Black
Color code	: Black
- Color code 4 x 5 mm, dari tepi atas 12 mm	

Packing condition, if applicable:	
Length of alufoil	: -
Pcs per roll / sheet	: -
Pcs perbundle	: 100 pcs
Pcs pershipper	: -
Other condition (*eg. Folded leaflet*)	: Lipat 2,Lipat 2, Lipat 2, Lipat 2 tengah
Revision History	: New Design
- Safety Update RSI Ver 3.0	
Prepared by	: ferry

REFERENCE DATE :

File name : Gentacortin Insert (10470505356V02)

DISETUJUI OLEH BPOM: 03/03/2021

ID REG: EREG100149VR12000310

Pregnancy
There are limited data from the use of Fluprednidene-21-acetate in pregnant women.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development.

The relevance of this finding to humans has not been established. Administration of Fluprednidene-21-acetate during pregnancy should only be considered if the expected benefit to the mother outweighs the risk to the foetus. The minimum quantity should be used for the minimum duration.

Breast feeding
The safe use of topical corticosteroids during lactation has not been established.

It is not known whether the topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable amounts in breast milk.

Administration of Fluprednidene-21-acetate during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.
If used during lactation Fluprednidene-21-acetate should not be applied to the breasts to avoid accidental ingestion by the infant.

3.7 Effects on Ability to Drive and Use Machines
There have been no studies to investigate the effect of Fluprednidene-21-acetate on driving performance or the ability to operate machinery. A detrimental effect on such activities would not be anticipated from the adverse reaction profile of topical Fluprednidene-21-acetate.

3.8 Undesirable Effects
Fluprednidene-21-acetate
Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and < 1/10), uncommon (≥1/1,000 and <1/100), rare (≥1/10,000 and 1<1,000) and very rare (<1/10,000), including isolated reports.

Post-marketing data
Infections and infestations
Very rare — Opportunistic infections

Immune System Disorders
Very rare — Local Hypersensitivity

Endocrine disorders
Very rare — Hypothalamic-pituitary adrenal (HPA) axis suppression: Cushingoid features: (e.g. moon face, central obesity), delayed weight gain/growth retardation in children, osteoporosis, glaucoma, hyperglycaemia/glucosuria, cataract, hypertension, increased weight/obesity, decreased endogenous cortisol levels, alopecia, trichorrhexis

Skin and Subcutaneous Tissue Disorders
Common — Pruritus, local skin burning/skin pain
Uncommon — Skin atrophy*, striae*, telangiectasias*
Very rare — Skin thinning*, skin wrinkling* skin dryness*, pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, allergic contact dermatitis/dermatitis, pustular psoriasis, erythema, rash, urticaria, acne

General Disorders and Administration Site Conditions
Very rare — Application site irritation/pain

Eye Disorders
Not known — Vision, blurred (see also section Special Warnings and Special Precautions for Use)

*Skin features secondary to local and/or systemic effects of hypothalamic-pituitary adrenal (HPA) axis supression.

Gentamicin sulfate
Ear and labyrinth disorders
Damage to the Nervus statoacusticus (N VIII) is possible which may affect the vestibular as well as the auditory organs.

Among the ototoxic reactions, vestibular disturbances are predominant.

Irreversible hearing loss and deafness was reported. Hearing disorders affect first of all the high frequency tone range and are usually irreversible. Pre-existing renal failure is the most important risk factor; furthermore, the risk increases with the quantity of the total and daily dose.
Symptoms of ototoxic effects include, for example, dizziness, tinnitus, reduced hearing capacity.

Renal and urinary disorders
Disturbances of renal function occur frequently under Gentamicin. Disturbances of renal function, such as an impaired glomerular filtration rate, are observed in about 10% of patients treated with Gentamicin and are usually reversible. The most important risk factors include high total dose, long duration of therapy, increased serum gentamicin concentrations (high trough levels); age, hypovolaemia and shock may constitute additional risks.

Clinical symptoms of renal damage include: proteinuria, cylindruria, haematuria, oliguria, increased serum creatinine and urea concentrations. Acute renal failure may develop in individual cases.

Very rare: Fanconi-like syndrome in patients treated with a prolonged course of high-dose Gentamicin

3.9 Overdose
Fluprednidene-21-acetate
Symptoms
Acute overdosage is very unlikely to occur. However, in the case of chronic overdosage or misuse, the features of hypercortisolism may occur.

Management
In the event of overdose, Fluprednidene-21-acetate should be withdrawn gradually by reducing the frequency of application or by substituting a less potent corticosteroid because of the risk of glucocorticosteroid insufficiency.

Further management should be as clinically indicated.

Gentamicin sulfate
Excessive prolonged use of topical gentamicin may lead to overgrowth of lesions by fungi or nonsusceptible bacteria.

Treatment: Appropriate antifungi or antibacterial therapy is indicated if overgrowth occurs.

4. PHARMACOLOGICAL PROPERTIES
4.1 Pharmacodynamic Properties
Mechanism of Action
The active ingredients of Gentacortin are:
- Fluprednidene-21-acetate is a very potent corticosteroid which has been synthesized by E. Merck's Hormone Research Department and which has ideal properties for local treatment of dermatological diseases: Intensive antiphlogistic, antiexudative and antipruritic action; rapid onset of action; prolonged effect and absence of systemic effects.
- Gentamicin sulfate, has a bactericidal effect on all sensitive gram-negative and gram-positive pathogens, in the stages of both proliferation and rest. The mechanism of action is based on a quantitative inhibition of protein synthesis and a qualitative effect by the incorporation of incorrect amino acids (misreading).

A modern mixed type base of Gentacortin is between o/w and w/o emulsion and is suitable for either dry eczema or wet eczema.

5. PHARMACEUTICAL PARTICULARS
5.1 List of Excipients
Vaseline white, Tween 40, Glycerol monostearate, Cetostearyl alcohol, Miglyol 812, Viscous paraffin, Propylene glycol, Aerosil, Sodium hydroxide, Sorbic acid, Rose fragrance, Purified water

5.2 Shelf-life
The expiry date is indicated on the packaging.

5.3 Special Precautions for Storage
Store at temperature below 30°C.

5.4 Package Quantities and Registration Number
Gentacortin Cream — Box, 1 tube @ 10 g — Reg. No. DKL8915802829A1

HARUS DENGAN RESEP DOKTER

Manufactured by
PT Meprofarm,
Bandung, Indonesia

Under license from
Merck Healthcare KGaA,
Darmstadt, Germany

For
PT Merck Tbk,
Jakarta, Indonesia

PI based on RSI Ver 3.0
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Kode supplier