Summary of Product Characteristics

1. Name of the Medicinal Product

Brand Name:
Cosvate - G
Generic Name:
Clobetasol Propionate and Gentamicin Cream

2. Qualitative and Quantitative Composition

Clobetasol Propionate BP ..... 0.05% w/w
Gentamicin (as Gentamicin Sulphate BP).....0.1% w/w
Chlorocresol BP (as preservative).....0.1% w/w
in a non-greasy base.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Cream for topical administration.

4. Clinical particulars

4.1 Therapeutic indications:

COSVATE G Cream is a super-high potency corticosteroid formulation indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses in which secondary bacterial infection is present, suspected or likely to occur. Treatment beyond 2 consecutive weeks is not recommended and the total dosage should not exceed 50 g/week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis.

4.2 Posology and method of administration

Posology

Apply a thin layer of COSVATE G Cream to the affected skin areas twice daily and rub it gently and completely. Treatment should be limited to 2 consecutive weeks and amounts greater than 50 g/week should not be used. COSVATE G Cream should not be used with occlusive dressings.

Route of administration: Cutaneous

Creams are especially appropriate for moist or weeping surfaces.

Adults, Elderly and Children over 1 year

Apply thinly and gently rub in using only enough to cover the entire affected area once or twice a day until improvement occurs (in the more responsive conditions this may be within a few days), then reduce the frequency of application or change the treatment to a less potent preparation. Allow adequate time for absorption after each application before applying an emollient.

Repeated short courses of clobetasol propionate may be used to control exacerbations.

In more resistant lesions, especially where there is hyperkeratosis, the effect of clobetasol can be enhanced, if necessary, by occluding the treatment area with polythene film. Overnight occlusion only is usually adequate to bring about a satisfactory response. Thereafter improvement can usually be maintained by application without occlusion.

If the condition worsens or does not improve within 2-4 weeks, treatment and diagnosis should be re-evaluated.

Treatment should not be continued for more than 4 weeks. If continuous treatment is necessary, a less potent preparation should be used.

The maximum weekly dose should not exceed 50 gms/week.

Therapy with clobetasol should be gradually discontinued once control is achieved and an emollient continued as maintenance therapy.

Rebound of pre-existing dermatoses can occur with abrupt discontinuation of clobetasol.

Recalcitrant dermatoses: Patients who frequently relapse

Once an acute episode has been treated effectively with a continuous course of topical corticosteroid, intermittent dosing (once daily, twice weekly, without occlusion) may be considered. This has been shown to be helpful in reducing the frequency of relapse.

Application should be continued to all previously affected sites or to known sites of potential relapse. This regimen should be combined with routine daily use of emollients. The condition and the benefits and risks of continued treatment must be re-evaluated on a regular basis.

Paediatric population

Cosvate G Cream is contraindicated in children under one year of age.

Children are more likely to develop local and systemic side effects of topical corticosteroids and, in general, require shorter courses and less potent agents than adults.

Care should be taken when using clobetasol propionate to ensure the amount applied is the minimum that provides therapeutic benefit.

Duration of treatment for children and infants

Courses should be limited if possible to five days and reviewed weekly. Occlusion should not be used.

Application to the face

Courses should be limited to five days if possible and occlusion should not be used.

Elderly

Clinical studies have not identified differences in responses between the elderly and younger patients. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption occurs. Therefore the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

Renal / Hepatic Impairment

In case of systemic absorption (when application is over a large surface area for a prolonged period) metabolism and elimination may be delayed therefore increasing the risk of systemic toxicity. Therefore the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

Method of administration

Cutaneous use. For external use only.

4.3 Contraindications

COSVATE G Cream is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations. Special warnings and precautions for use

Special Warnings and Precautions:

General: COSVATE G Cream should not be used in the treatment of rosacea or perioral dermatitis, and should not be used on the face, groin, or axillae. Systemic absorption of topical corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal from treatment. Patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. Recovery of HPA axis function is generally prompt upon discontinuation of topical corticosteroids. Paediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios.

Information for Patients: Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the Physician. It is

for external use only. Avoid contact with the eyes.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged, otherwise covered, or wrapped so as to be occlusive unless directed by the Physician.
4. Patients should report any signs of local adverse reactions to the Physician.

Pregnancy: Pregnancy Category C. COSVATE G Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Paediatric Use: Use in Paediatric patients under 12 years of age is not recommended.

Nursing Mothers: It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Nevertheless, a decision should be made whether to discontinue the drug, taking into account the importance of the drug to the mother.

4.4 Special warnings and precautions for use

Cases of osteonecrosis serious infections (including necrotizing fasciitis) and systemic immunosuppression (sometimes resulting in reversible Kaposi's sarcoma lesions) have been reported with long-term use of clobetasol propionate beyond the recommended doses (see section 4.2). In some cases patients used concomitantly other potent oral/topical corticosteroids or immunosuppressors (e.g. methotrexate, mycophenolate mofetil). If treatment with local corticosteroids is clinically justified beyond 4 weeks, a less potent corticosteroid preparation should be considered.

Clobetasol should be used with caution in patients with a history of local hypersensitivity to other corticosteroids or to any of the excipients in the preparation. Local hypersensitivity reactions (see section 4.8) may 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 4.8).

Cosvate G Cream contains:

• 475 mg propylene glycol per gram of product. Propylene glycol may cause skin irritation.
• cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).
• chlorocresol which may cause allergic reactions.

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.

Paediatric population
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.

Duration of treatment for children and infants
Courses should be limited if possible to five 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.

Use in Psoriasis
Topical corticosteroids should be used with caution in psoriasis as rebound relapses, development of tolerances, risk of generalised 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.

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.

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.

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 5 days.

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. If clobetasol does enter the eye, the affected eye should be bathed in copious amounts of water.

Visual disturbance
Visual disturbance has been 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.
Cosvate G cream contains paraffin. Instruct patients not to smoke or go near naked flames due to the risk of severe burns. Fabric (clothing, bedding, dressings etc) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

Topical steroid withdrawal syndrome
Long term use of topical steroids can result in the development of rebound flares after stopping treatment (topical steroid withdrawal syndrome). A severe form of rebound flare can develop which takes the form of a dermatitis with intense redness, stinging and burning that can spread beyond the initial treatment area. It is more likely to occur when delicate skin sites such as the face and flexures are treated. Should there be a reoccurrence of the condition within days to weeks after successful treatment a withdrawal reaction should be suspected. Reapplication should be with caution and specialist advise is recommended in these cases or other treatment options should be considered.
The label will state very strong steroid.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. Interactions with systemically administered medicinal products are considered minimal.

4.6 Fertility, pregnancy and lactation Pregnancy

Pregnancy: Pregnancy Category C.

COSVATE G Cream should be used during pregnancy only if the

potential benefit justifies the potential risk to the foetus. **Nursing Mothers:** It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Nevertheless, a decision should be made whether to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

COSVATE G cream has no or negligible influence on the ability to drive or to use machines.

4.8 Undesirable effects

The estimation of the frequency of undesirable effects is based on a pooled analysis of data from clinical studies and spontaneous reporting.
The most frequently reported adverse reaction during treatment is pruritus. Undesirable effects are listed by MedDRA SOC and the individual undesirable effects are listed starting with the most frequently reported. Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.
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 Very
rare
<1/10,000
Not known (cannot be estimated from the available data)

Immune system disorders	
Uncommon: (≥1/1,000 and <1/100)	Hypersensitivity
Eye disorder	
Not known	Vision, blurred*
Skin and subcutaneous tissue disorders	
Uncommon: (≥1/1,000 and <1/100)	Dermatitis contact Eczema (condition aggravated) Skin burning sensation Pruritus Dry skin

Rare: (≥1/10,000 and <1/1,000)	Erythema Urticari a Rash (including rash erythematous and rash generalised)
General disorders and administration site conditions	
Uncommon: (≥1/1,000 and <1/100)	Application site pain Application site irritation
Rare: (≥1/10,000 and <1/1,000)	Application site swelling Application site vesicles

*See also section 4.4
Systemic undesirable class effects of corticosteroids like betamethasone valerate include adrenal suppression especially during prolonged topical administration (see section 4.4).

Raised intra-ocular pressure, glaucoma or cataract may also occur after topical use of corticosteroids near the eyes, particularly with prolonged use and in patients predisposed to developing glaucoma and cataract (see section 4.4).
Dermatological undesirable class effects of potent corticosteroids include: Atrophy, dermatitis (including dermatitis contact and dermatitis acneiform), perioral dermatitis, skin striae, telangiectasia, rosacea, erythema, hypertrichosis, hyperhidrosis and depigmentation. Ecchymosis may also occur with prolonged use of topical corticosteroids.
Class effects for corticosteroids have been uncommonly reported for Futop B cream as described in the frequency table above.
Paediatric population
The observed safety profile is similar in children and adults (see section 4.4).

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 pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 OVERDOSAGE:
Topically applied COSVATE G Cream can be absorbed in sufficient amounts and does not produce systemic effects

5 Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: D07CC01, corticosteroids (Group III) and antibiotics in combination, for external use.
ATC code: D07CC01.
Cosvate G cream combines the well-known anti-inflammatory and antipruritic effects of betamethasone with the potent topical antibacterial action of fusidic acid. Betamethasone valerate is a topical steroid rapidly effective in those inflammatory dermatoses which normally respond to this form of therapy. More refractory conditions can often be treated successfully. When applied topically, fusidic acid is effective against Staphylococcus aureus, Streptococci, Corynebacteria, Neisseria and certain Clostridia and Bacteroides. Concentrations of 0.03 to 0.12 microgram per ml inhibit nearly all strains of S. aureus. The antibacterial activity of fusidic acid is not diminished in the presence of betamethasone.

Mechanism of Action:
Clobetasol Propionate has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.
Gentamicin is an aminoglycoside antibiotic indicated in the treatment of gram-positive as well as gram-negative infections. Gentamicin is effective against most gram-negative

organisms including *E coli, Klebsiella pneumoniae, Enterobacter aerogenes, Serratia marcescens* and *Citrobacter freundii*.

5.2 Pharmacokinetic properties
There are no data which define the pharmacokinetics of Futop B cream, following topical administration in man.
However, *in vitro* studies show that fusidic acid can penetrate intact human skin. The degree of penetration depends on factors such as the duration of exposure to fusidic acid and the condition of the skin. Fusidic acid is excreted mainly in the bile with little excreted in the urine.
Betamethasone is absorbed following topical administration. The degree of absorption is dependent on various factors including skin condition and site of application. Betamethasone is metabolised largely in the liver but also to a limited extent in the kidneys, and the inactive metabolites are excreted with the urine

5.3 Preclinical Safety data:
Studies of corticosteroids in animals have shown reproductive

toxicity (e.g., cleft palate, skeletal malformations, low birth weight).

6 Pharmaceutical particulars:

6.1 List of Excipients

Disodium EDTA, Propylene Glycol, White soft Paraffin, Cetostearyl Alcohol, Cetomacrogol–1000, Liquid Paraffin (Light), Chlorocresol, Dibasic potassium Phosphate & Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C in a dry and dark place. DO NOT FREEZE.

6.5 Nature and contents of container

The cream is filled in printed laminated tubes with internal lacquer coating and HDPE screw-on caps and enclosed in an outer carton along with pack insert.

Pack sizes available are 5 g and 15 g. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No Special requirements.

7.0 Marketing Authorization Holder Eris Oaknet Healthcare Pvt. Ltd.

3rd Floor, A Wing, Shilp Accord, Opp. Time Square II, Thaltej, Ahmedabad – 380054, Gujarat, India.

Manufactured by:

Curetech Skincare
At: Plot No. 33 & 34, Phase-IV, Bhatoli Kalan, Baddi, Distt Solan, Himachal Pradesh – 173 205, India.

8.0 Marketing Authorization Numbers
16653

9.0 Date of first authorization/renewal of the authorization
Date of First Authorization: 08/10/2018

10.0 Date of revision of the text
11/08/2026