Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

Clobamol cream

2. Qualitative and quantitative composition

Clobetasol Propionate 0.05% w/w
Clotrimazole 1.0% w/w

Excipients with known effect:
Propylene glycol
For the full list of excipients, see section 6.1

3. Pharmaceutical form

Topical Cream

A white to off white smooth perfumed cream

4. Clinical particulars

4.1 Therapeutic indications

Clobetasol propionate is a very active topical corticosteroid which is of particular value when used in short courses for the treatment of more resistant dermatoses such as psoriasis (excluding widespread plaque psoriasis) , recalcitrant eczemas, lichen planus, discoid lupus erythematosus, and other skin conditions which do not respond satisfactorily to less active steroids. Clotrimazole is indicated for the topical treatment of candidiasis due to Candida albicans and Tinea versicolor due to Malassezia furfur gel is also indicated for the topical treatment of the following dermal infections : Tinea pedis, Tinea cruris and Tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes , Epidermophyton floccosum and Microsporum canis.

4.2 Posology and method of administration

Apply sparingly to the affected area once or twice daily until improvement occurs. As with other highly active topical steroid preparations, therapy should be discontinued when control is achieved. In the more responsive conditions this may be within a few days. If no improvement is seen within two to four weeks, reassessment of the diagnosis, or referral, may be necessary. Repeated short courses of Clobetasol Propionate & Clotrimazole Cream may be used to control exacerbations. If continuous steroid treatment is necessary, a less potent preparation should be used. In very resistant lesions, especially where there is hyperkeratosis, the anti-inflammatory effect of Clobetasol Propionate & Clotrimazole Cream 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. Gently massage sufficient Clobetasol Propionate & Clotrimazole Cream into the affected and surrounding skin areas twice a day in the morning and evening. Clinical improvement with relief of pruritus usually occurs within the first week of treatment with Clobetasol Propionate & Clotrimazole Cream. If the patient shows no clinical improvement after 4 weeks of treatment with Clobetasol Propionate & Clotrimazole Cream the diagnosis should be reviewed.
Method of administration: For Topical application.

4.3 Contraindications

- Rosacea
- Acne vulgaris
- Perioral dermatitis
- Perianal and genital pruritus
- Primary cutaneous viral infections (e.g. herpes simplex, chickenpox)
- Hypersensitivity to the preparation
- The use of Clobetasol Propionate & Clotrimazole Cream skin preparations is not indicated

in the treatment of primary infected skin lesions caused by infection with fungi (e.g. candidiasis, tinea) or bacteria (e.g. impetigo); or dermatoses in children under one year of
age, including dermatitis and napkin eruptions.

4.4 Special warnings and precautions for use

Long-term continuous therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion. If Clobetasol Propionate & Clotrimazole Cream is required for use in children, it is recommended that the treatment should be reviewed weekly. It should be noted that the infant's napkin may act as an occlusive dressing. If used in childhood or on the face, courses should be limited if possible to five days and occlusion should not be used. The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis, discoid lupus erythematosus and severe eczema. If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result. If Clobetasol Propionate & Clotrimazole Cream gel does enter the eye, the affected eye should be bathed in copious amounts of water. Topical steroids may be hazardous in psoriasis for a number of reasons including 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. If used in psoriasis careful patient supervision is important. 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 systemic administration of antimicrobial agents. Bacterial infection is encouraged by the warm,

moist conditions induced by occlusive dressings, and so the skin should be cleansed before a fresh dressing is applied. 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. Clobetasol Propionate & Clotrimazole Cream contains cetostearyl alcohol which can cause local skin reactions (e.g. contact dermatitis), propylene glycol which may cause skin irritation and chlorocresol which may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Clotrimazole

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.

Clobetasol

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.

4.6 Fertility, pregnancy, and lactation

Pregnancy:

There are limited data from the use of clobetasol in pregnant women.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development (see Nonclinical Information)

The relevance of this finding to humans has not been established. Administration of clobetasol 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.

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 or midwife.

Breast-feeding:

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.

Fertility:

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.

4.7 Effects on ability to drive and use machines.

The medicinal product has no influence on the ability to drive or operate machinery.

4.8 Undesirable effects

Clobetasol

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 infection

Immune System Disorders

Very rare	Hypersensitivity, generalised rash

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, hyperglycaemia/glucosuria, 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\
Not known	Withdrawal reactions - redness of the skin which may extend to areas beyond the initial affected area, burning or stinging sensation, itch, skin peeling, oozing pustules. (see section 4.4)

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

General Disorders and Administration Site Conditions

Very rare	Application site irritation/pain

Eye disorders

Very rare	Cataract, central serous chorioretinopathy, glaucoma

Not known (cannot be estimated from available data)	Vision, blurred

Clotrimazole

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, dermatitis contact, erythema, parasthesia, skin exfoliation, pruritus, rash, urticaria, stinging skin/burning sensation skin.
General disorders and administration site conditions: application site irritation, application site reaction, oedema, pain.

Reporting of suspected adverse reactions: 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 Overdose

Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse, the features of hypercortisolism may appear and in this situation topical steroids should be reduced or discontinued gradually, under medical supervision. 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.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Clobetasol propionate is a highly active corticosteroid with topical anti-inflammatory activity. The major effect of clobetasol propionate on skin is a non-specific anti-inflammatory response, partially due to vasoconstriction and decrease in collagen synthesis. Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergostero 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.

5.2 Pharmacokinetic properties

Percutaneous penetration of clobetasol propionate varies among individuals and can be increased by the use of occlusive dressings, or when the skin is inflamed or diseased. Mean peak plasma clobetasol propionate concentrations of 0.63 ng/ml occurred in one study eight hours after the second application (13 hours after an initial application) of 30 g clobetasol propionate 0.05% ointment to normal individuals with healthy skin. Following the application of a second dose of 30 g clobetasol propionate cream 0.05% mean peak plasma concentrations were slightly higher than the ointment and occurred 10 hours after application. In a separate study, mean peak plasma concentrations of approximately 2.3 ng/ml and 4.6 ng/ml occurred respectively in patients with psoriasis and eczema three hours after a single application of 25 g clobetasol propionate 0.05% ointment. Following percutaneous absorption of clobetasol propionate, the drug probably follows the metabolic pathway of systemically administered corticosteroids, i.e. metabolised primarily by the liver and then excreted by the kidneys. However, systemic metabolism of clobetasol has never been fully characterised or quantified. 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.

5.3 Preclinical safety data

Not applicable.

6. Pharmaceutical particulars

6.1 List of excipients

Cetomacrogol 1000 INH
Cetostearyl alcohol BP
White Soft Paraffin BP
Methyl Paraben BP
Propyl Paraben BP
Sodium Acid Phosphate BP
Disodium Acid Phosphate BP
Propylene Glycol BP
Light Liquid Paraffin BP
Isopropyl Myristate BP
Perfume
Dimethicone 100 BP
Purified water BP

6.2 Incompatibilities
None known

6.3 Shelf life
36 months

6.4 Special precautions for storage:
Store at temperature not exceeding 30°C; do not freeze.

6.5 Nature and contents of container
A Lami tube, with a membrane seal at the nozzle, internal epoxy lacquer, latex end seal band in the crimp seal and a white plastic cap for reclosure after piercing membrane. Pack sizes: The cream is filled into lami tubes with white colour stand-up caps and enclosed in an outer carton. Pack sizes available are 30g , 20 gm & 15gm.

6.6 Special precautions for disposal and other handling:
Not applicable.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:
Kremoint Pharma Pvt. Ltd., B-8 Additional MIDC, Ambernath Ambernath (E) Thane 421506
Manufacturing site address:
Kremoint Pharma Pvt Ltd situated at B-8, Additional Ambernath MIDC, Anandnagar, Ambernath (East), Dist. Thane 421 506. Maharashtra, India KD-146 and KD-171.

8. Marketing authorization number
H2024/CTD9355/20632

9. Date of first registration
16/02/2024

10. Date of revision of the text:

November 2024