Applicant:	Galderma Laboratories South Africa (Pty) Ltd
Proprietary name:	CLOBEX® SPRAY
Dosage form and strength:	Spray (0,5 mg/g Clobetasol propionate)
Registration Number	46/13.4.1/0556

PROFESSIONAL INFORMATION

SCHEDULING STATUS: **S4**

1. NAME OF THE MEDICINE

Spray solution

CLOBEX® SPRAY

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

CLOBEX® SPRAY contains 0.5% w/w (500 µg/g) clobetasol propionate

CLOBEX® SPRAY excipients: ethanol (49,25 % w/w), isopropyl myristate, sodium laurilsulfate and undecylenic acid.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

CLOBEX® SPRAY: Clear colourless solution with no particulate matter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CLOBEX® SPRAY is indicated for the topical treatment of moderate to severe plaque-type psoriasis in adults.

4.2 Posology and method of administration

Posology

For application to the skin:

CLOBEX® SPRAY should be sprayed directly onto the affected areas twice daily. It should be rubbed in gently until completely absorbed. Hands should be washed carefully after application.

The period of treatment should be limited to 4 weeks and must be adjusted to suit the individual patient. (see section 4.4). If further treatment with a topical corticosteroid is required after 4 weeks of treatment with **CLOBEX® SPRAY**, a less potent steroid should be used. Treatment with **CLOBEX® SPRAY** should be stopped if disease control is achieved.

After a period off treatment with **CLOBEX® SPRAY**, the treatment may be repeated to treat exacerbations of psoriasis.

Not more than 50 g of cutaneous spray solution should be used per week.

Paediatric population

The safety and efficacy of **CLOBEX® SPRAY** in children and adolescents under 18 years of age have not been established.

4.3 Contraindications:

Hypersensitivity to **CLOBEX® SPRAY** or to any of the excipients of **CLOBEX® SPRAY**.

Skin areas affected by bacterial, viral (varicella, herpes simplex, herpes zoster), fungal or parasitic infections and specific skin diseases (skin tuberculosis, skin diseases caused by syphilis).

Acne vulgaris, rosacea or perioral dermatitis (see section 4.8.)

CLOBEX® SPRAY must not be applied to the eyes and eyelids (risk of glaucoma, risk of cataract) or to ulcerous wounds.

Peri-anal and genital pruritus.

Pregnancy and Lactation (see section 4.6)

Use in children

Safety and efficacy has not been established in subjects younger than 18 years of age. (See section 4.4)

4.4 Special warnings and precautions for use

Clobetasol propionate belongs to the most potent class of topical corticosteroids (Group IV) and prolonged use may result in serious undesirable effects. If treatment with a local corticosteroid is clinically justified beyond 4 weeks, a less potent corticosteroid preparation should be considered. Repeated but short courses of clobetasol propionate may be used to control exacerbations.

Treatment of psoriasis with **CLOBEX® SPRAY** (or its withdrawal) may provoke generalised pustular psoriasis in case of intensive and prolonged topical use. Hypersensitivity to **CLOBEX® SPRAY** may occur. This can be suspected in case of resistance to treatment. **CLOBEX® SPRAY** is not recommended in patients who are hypersensitive to other corticosteroids.

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 other potent oral/topical corticosteroids or immunosuppressive medicines concomitantly (e.g. methotrexate, mycophenolate mofetil). If treatment with local corticosteroids is clinically justified beyond 4 weeks, a less potent corticosteroid preparation should be considered.

Treatment of large surface areas, long-term continuous therapy with **CLOBEX® SPRAY** or use of occlusive dressings can enhance absorption and lead to a higher risk of systemic effects. Systemic absorption of topical corticosteroids has caused reversible adrenal suppression with the potential for glucocorticosteroid insufficiency, manifestations of Cushing’s syndrome, hyperglycaemia, and glycosuria in some patients. Medical supervision should be increased and patients should be evaluated periodically

for evidence of hypothalamic-pituitary-adrenal axis suppression. Such systemic effects usually resolve when treatment is stopped.

Abrupt discontinuation can lead to acute adrenal insufficiency.

CLOBEX® SPRAY is not recommended for use on the eyelids, intertriginous areas (axillae and genito-anal regions) and on other erosive skin surfaces as this could increase the risk of topical adverse events such as atrophic changes, telangiectasia or cortico-induced dermatitis.

If **CLOBEX® SPRAY** does enter the eye, the affected eye should be rinsed with copious amounts of water.

Patients with severe liver dysfunction and severe diabetes mellitus should be treated with special caution and closely monitored for side-effects.

CLOBEX® SPRAY should be used with caution for a number of reasons including post treatment rebound, relapses, development of tolerance (tachyphylaxis) and development of local or systemic toxicity such as atrophy, infection and telangiectasia of the skin or hypothalamic-pituitary-adrenal axis suppression.

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.

Paediatric population

Safety and efficacy has not been established in subjects younger than 18 years of age.

4.5 INTERACTIONS with other medicines and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy has not been established.

There are no adequate data from the use of **CLOBEX® SPRAY** in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown. As a precautionary measure, **CLOBEX® SPRAY** should not be used during pregnancy (see section 4.3)

Lactation

Systemically administered corticosteroids pass into breast milk.

CLOBEX® SPRAY should not be prescribed to women breastfeeding their infants (see section 4.3)

Fertility

Clobetasol propionate decreased fertility when administered subcutaneously to rats.

4.7 Effects on ability to drive and the use of machines

As a topical corticosteroid, **CLOBEX® SPRAY** has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The most commonly reported adverse reaction in clinical trials was application site burning, experienced in 47,9 % of subjects with **CLOBEX® SPRAY**. Less frequent adverse reactions were application site atrophy, telangiectasia, application site folliculitis, which occurred respectively in 3,6 %, 2,8 % and 2,6 % of subjects treated with **CLOBEX® SPRAY**.

All these reactions usually resolved spontaneously.

If signs of local intolerance appear, application should be suspended until they disappear. If signs of hypersensitivity appear, application should be stopped immediately.

Adverse reactions reported in clinical trials and post marketing surveillance, ordered by System Organ Class and Preferred Terms and presented by absolute frequency:

Table 1: Adverse reactions reported in clinical trials:

System Organ Class	**Incidence**	**Preferred Terms**
Skin and subcutaneous tissue disorders	Very common (≥1/10)	Application site burning
	Common (≥1/100 to <1/10)	Application site atrophy, Application site folliculitis, Application site pain, Application site irritation Telangiectasia
	Uncommon (≥1/1,000 to <1/100)	Application site pruritus, Application site dryness Rash Erythema
	Rare (≥1/10,000 to <1/1,000)	Skin discolouration
Eye disorder	Not known	Vision, blurred (see section 4.4)

Table 2: Adverse reactions reported in post marketing surveillance:

System Organ Class	**Incidence**	**Preferred Terms**
Immune System Disorders	Uncommon (≥1/1,000 to <1/100)	Hypersensitivity
Endocrine disorders	Uncommon (≥1/1,000 to <1/100)	Adrenal suppression Cushing syndrome
Skin and subcutaneous tissue disorders	Uncommon (≥1/1,000 to <1/100)	Allergic contact dermatitis Psoriasis (aggravation)

Prolonged use of **CLOBEX® SPRAY** treatment of extensive areas or use of large amounts can result in sufficient systemic absorption to produce the features of hypercortisolism (Cushing's syndrome) or of Hypothalamus-Pituitary-Adrenal (HPA) axis suppression. Such effects are more likely to occur if occlusive dressings or bandages are used.

Prolonged and/or intensive treatment with **CLOBEX® SPRAY** may cause local changes, such as local skin atrophy, striae, telangiectasia, erythema, purpura, contact dermatitis especially with the use of occlusive dressings.

When applied to the face, **CLOBEX® SPRAY** can induce perioral dermatitis, skin atrophy or worsen rosacea.

There are reports of pigmentation changes, acne, pustular eruptions and hypertrichosis with **CLOBEX® SPRAY.**

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to

report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form,"** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Acute overdose is unlikely to occur, however, in the case of chronic overdose or misuse, the features of hypercortisolism may appear and in this situation, treatment should be discontinued gradually. However, because of the risk of acute adrenal suppression, this should be done under medical supervision.

Treatment is symptomatic and supportive.

In cases where **CLOBEX® SPRAY** is accidentally swallowed, a healthcare professional should be consulted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 13.4.1 Dermatological preparations – Antipruritics, Corticosteroids with or without anti-infective agents.

Clobetasol propionate is a potent corticosteroid which has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of topical corticosteroids in general is unclear. However, corticosteroids are thought to act by 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.

5.2 Pharmacokinetic properties

No specific study was performed (in vivo or in vitro) with clobetasol propionate 500 micrograms/g cutaneous spray, solution.

In vitro studies in human skin with different formulations of clobetasol propionate demonstrated that clobetasol propionate was recovered mainly in the epidermis (including stratum corneum).

Once absorbed through the skin, topical corticosteroids are handled through metabolic pathways similar to systemically administered corticosteroids, i.e. metabolised primarily by the liver and then excreted by the kidneys.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

CLOBEX® SPRAY:

Ethanol (96%)

Isopropyl myristate,

Sodium laurilsulfate,

Undecylenic acid.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in the original package.

Store at or below 30 °C. Do not refrigerate or freeze.

Do not remove the bottle from the carton until required for use.

Discard 3 months after first opening.

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.

Applicant:	Galderma Laboratories South Africa (Pty) Ltd
Proprietary name:	CLOBEX® SPRAY
Dosage form and strength:	Spray (0,5 mg/g Clobetasol propionate)
Registration Number	46/13.4.1/0556

6.5 Nature and contents of container

CLOBEX® SPRAY is presented in white high density polyethylene bottles with a white polypropylene cap and a spray pump containing 30 ml, 60 ml or 120 ml of spray solution, packed in a carton box.

6.6 Special precautions for disposal

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION:

Galderma Laboratories South Africa (Pty) Ltd

Nicol Main Office Park

Block C, First Floor

FutureSpace

2 Bruton Road

Bryanston

2191

8. REGISTRATION NUMBER:

46/13.4.1/0556

9. DATE OF FIRST AUTHORISATION

29 July 2016

10. DATE OF REVISION OF THE TEXT

01 September 2022