SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

XYNTAVATE GEL

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1. NAME OF THE MEDICINAL PRODUCT

XYNTAVATE GEL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Clobetasol Propionate USP 0.05%
Excipients Q.s. (For full list of excipients, see section 6.1)

3. PHARMACEUTICAL FORM

Colorless and odorless transparent gel.
Presentation: Aluminium Tube of 25g.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Xyntavate gel is a dermatological product indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

4.2 Posology and method of administration

Xyntavate gel is a Prescription Only Medicine for dermatological use.
It is to be used as directed by the physician.

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

Method of administration
For EXTERNAL USE ONLY.
Apply with a gentle rub to the affected area as directed by the physician.
The treated skin area should not be bandaged, otherwise covered or wrapped, so as to be occlusive unless directed by the physician.
Treatment beyond 2 consecutive weeks is not recommended and the total dosage should not exceed 50g per week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis.

As with other highly active corticosteroids, therapy should be discontinued when control has been achieved.
If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary.

4.3 Contraindications:

Xyntavate gel is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.
Xyntavate gel should not be used in the treatment of rosacea or perioral dermatitis and it should not be used on the face, groin, or axillae.

4.4 Special warnings and precautions for use

Clobetasol Propionate is a topical corticosteroid that has been shown to suppress the HPA axis at doses as low as 2g per day.
The skin should be cleaned before fresh dressing is applied.
Bacterial infections are encouraged by the warm, moist conditions induced by occlusive dressings.

Long term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression, with or without clinical features of Cushing's syndrome can occur even without occlusion. In these situations, topical steroids should be discontinued gradually under medical supervision because of the risk of adrenal insufficiency.
Extension of infection may occur due to the masking effect of the steroid. Withdraw topical corticosteroids if there is a spread of infection.
Extended or recurrent application may increase the risk of contact sensitization.

4.5 Interactions with other medicinal products and other forms of interaction

The risk of topical corticosteroids interacting with other drugs is low, However the use of Clobetasol gel might interact with other topical medications that contain steroids and any drug that affects the immune system. The Doctor or Pharmacist is to be informed if using any of the above class of drugs.

4.6 Pregnancy and lactation

There are no adequate and well-controlled studies of the teratogenic potential of clobetasol propionate in pregnant women. Clobetasol propionate topical preparations should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when clobetasol propionate topical preparations are administered to a nursing woman.

4.7 Effect on ability to drive and use machines

None known.

4.8 Undesirable effects

In a controlled trial with Clobetasol Propionate for topical use, the only reported adverse reaction that was considered to be drug related was a report of burning sensation (1.8% of treated persons).
In a large controlled clinical trial with Clobetasol Propionate formulations, the most frequently reported reactions have included burning, stinging, irritation, pruritus, erythema, folliculitis, cracking and fissuring of the skin, numbness of the fingers, skin atrophy, and telan giectasia (all less than 2%).

Cushing's syndrome has been reported infrequently with topical corticosteroid, but may occur more frequently with super-high potency corticosteroids such as clobetasol propionate. These reactions are listed in an approximate decreasing order of occurrence: dryness, hypertricosis, acneiform eruptions, hypopigmentation, periora cerratitis, allergic contact dermatitis, secondary infection, irritation, striae and miliaria.

4.9 Overdose

Following topical application of XYNTAVATE GEL, clobetasol propionate can be absorbed in sufficient amounts to produce systemic effects (see special warnings and precautions).

Treatment in case of over-dosage

Product should be discontinued. Seek the physician.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

The pharmacodynamics of corticosteroids is well known and described in the scientific literature.

Topical corticosteroids act as anti-inflammatory agents via multiple mechanisms to inhibit late phase allergic reactions including decreasing the density of mast cells, decreasing chemotaxis and activation of eosinophils, decreasing cytokine production by lymphocytes, monocytes, mast cells and eosinophils, and inhibiting the metabolism of arachidonic acid. Corticosteroids modify the functions of epidermal and dermal cells and of leukocytes participating in proliferative and inflammatory skin diseases. After passage through the cell membrane corticosteroids react with receptor proteins in the cytoplasm to form a steroid-receptor complex. This complex moves into the nucleus, where it binds to DNA. The binding process then changes the transcription of messenger RNA (mRNA). Because mRNA acts as template for protein synthesis, corticosteroids can either stimulate or inhibit the synthesis of specific proteins. Thus corticosteroids are known to stimulate the production of a glycoprotein called lipocortin. The formed lipocortin inhibits the activity of phospholipase A2, which releases arachidonic acid, the precursor of prostanoids and leukotrienes, from phospholipids. In contrast, corticosteroids inhibit mRNA responsible for interleukin-1 formation. These actions of corticosteroids on arachidonic acid metabolism and interleukin-1 formation produce anti-inflammatory, immunosuppressive and anti-mitogenic effects.

5.2 Pharmacokinetic properties

Clobetasol Propionate can be absorbed from normal intact skin. Once absorbed through the skin, it is handled through pharmacokinetic pathways similar to systematically administered corticosteroids. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusion, inflammation and/or other disease processes in the skin may also increase percutaneous absorption.

Corticosteroids are bound to plasma proteins in varying degrees and metabolized primarily by the liver and are then excreted by the kidneys.

5.3 Clinical data

The indications applied for are similar to the authorized therapeutic indications for medicinal products with the same active substance which are the following:
Psoriasis (excluding plaque psoriasis), recalcitrant eczema, Lichen planus, discoid lupus erythematosus and other skin conditions that do not respond satisfactorily to less active steroids.
With regard to clinical treatment guidelines the following have been referred to:
Treatment of psoriasis

- European S3-Guidelines on the systemic treatment of psoriasis vulgaris.

Guidelines of care for the management and treatment of psoriasis with topical therapies (Nast et al. 2012, Pathirana et al. 2009, Murphy 2011).
American Academy of Dermatology Guidelines of care for the management of psoriasis and psoriatic arthritis (Menter et al. 2009).
Treatment of eczema

- The efficacy of '0.05% Clobetasol + 2.5% zinc sulphate' cream vs. '0.05% Clobetasol alone' cream in the treatment of the chronic hand eczema is compared in a double-blind study. (Faghihi et al. 2008).

Additional data on treatment practices of hand eczema are provided in Soost et al (2011).
Treatment of lichen planus
Efficacy is supported by clinical study data. Radfar et al (2008) present data from a comparative treatment study of topical tacrolimus and clobetasol in oral lichen planus. The general clinical practice for lichen planus is discussed in a review in the New England Journal (Le Cleach and Chosidow, 2012). Clinical practice in children is also discussed (Balasubramaniam et al, 2008; Pandhi et al,2013).
Treatment of lupus erythematodes
Efficacy of tacrolimus vs. clobetasol propionate in the treatment of facial cutaneous lupus erythematosus (data from a randomized, double blind, bilateral comparison study) is presented in Tzung et al (2007) and in therapy-resistant cutaneous lupus erythematosus: a cohort study (Madan et al 2009).

6. PHARMACEUTICAL PARTICULARS

6.1 List of ingredients

Active ingredient
Clobetasol Propionate

Excipients
Propylene Glycol
Carbomers
Triethanolammine
Methyl Paraben
Propyl Paraben
Water

6.2 Incompatibilities

No interaction has been reported on topical application with XYNTAVATE GEL. Avoid using other topical medications.

6.3 Shelf life

36 months from the date of production.

6.4 Special precautions for storage

Store in a cool, dry place at a temperature not exceeding 30°C. Do not freeze. Keep medicine out of reach of children.

6.5 Nature and content of container

Aluminium tube.
Presentation: Tube of 25g packed in a paper pack with leaflet.

6.6 Special precaution for disposal

N/A

7. APPLICANT / MANUFACTURER

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