PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

PrJAMP Clobetasol Spray

Clobetasol Propionate Topical Solution

Solution, 0.05% w / w, Topical

House Standard

Topical Corticosteroid

JAMP Pharma Corporation 1310 rue Nobel Boucherville, Québec J4B 5H3	Date of Initial Authorization: January 23, 2023

Submission Control Number: 232087

RECENT MAJOR LABEL CHANGES

Not Applicable	

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

JAMP Clobetasol Spray (clobetasol propionate topical solution) 0.05% is a super-high potent topical corticosteroid formulation indicated for the treatment of moderate to severe plaque psoriasis in subjects 18 years of age and older.

JAMP Clobetasol Spray (clobetasol propionate topical solution) 0.05% is not indicated for long-term use. Treatment should be limited to a maximum or four consecutive weeks. Intermittent use has not been studied.

1.1 Pediatrics

Use in patients under 18 years of age is not recommended. JAMP Clobetasol Spray is contraindicated in children under 2 years of age.

1.2 Geriatrics

Limited data are available in patients aged 65 years and over. Dosing selection should be made with caution in geriatric patients. See **7 WARNINGS AND PRECAUTIONS**, **7.1.4 Geriatrics**.

2 CONTRAINDICATIONS

- Patients who are hypersensitive to clobetasol propionate, to corticosteroids, or to any ingredient in the formulation or component of the container. For a complete listing, see the **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING** section of the Product Monograph.

- Patients with skin areas affected by bacterial or mycobacterial infections (including tuberculosis of the skin), fungal infections involving the skin, certain viral diseases such as herpes simplex, chickenpox, and vaccinia, parasitic infections or ulcerous wounds.

- Must not be used in children under 2 years of age.

- Must not be applied to the eyes and eyelids (risk of glaucoma, risk of cataract).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Treatment duration should not exceed 4 consecutive weeks.
- JAMP Clobetasol Spray 0.05% should not be used with occlusive dressings.

4.2 Recommended Dose and Dosage Adjustment

JAMP Clobetasol Spray (clobetasol propionate topical solution) 0.05% should be applied to the affected skin areas twice daily and rubbed in gently and completely. Wash hands carefully with water after application.

JAMP Clobetasol Spray 0.05% is a super-high potent topical corticosteroid formulation. Patients should be instructed to use JAMP Clobetasol Spray for the minimum amount of time necessary. Treatment should be limited to 4 consecutive weeks. Treatment beyond two weeks should be limited to localized lesions of moderate to severe plaque psoriasis that have not sufficiently improved after the initial two weeks of treatment with JAMP Clobetasol Spray 0.05%. If treatment with a local corticosteroid is clinically justified beyond 4 weeks, switching to a less potent corticosteroid preparation should be considered.

Total dosage of the product should not exceed 50 mL per week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis. Therapy should be discontinued when control has been achieved. If no improvement is seen within two weeks, reassessment of diagnosis may be necessary.

JAMP Clobetasol Spray (clobetasol propionate topical solution) 0.05% is not indicated for long-term use. Intermittent use has not been studied.

Pediatrics: Use in patients between 2 and 18 years of age is not recommended and is contraindicated in children below 2 years of age. See **1.1 Pediatrics**.

4.4 Administration

JAMP Clobetasol Spray 0.05% should be applied to the affected skin areas twice daily and rubbed in gently and completely.

How to use JAMP Clobetasol Spray:

The following instructions outline the proper use of JAMP Clobetasol Spray (clobetasol propionate topical solution) 0.05%. The Pump Top and Directional Spray Nozzle mechanism are described in the figure below (Fig.1).

Fig. 1

When you receive JAMP Clobetasol Spray, the Directional Spray Nozzle is in the "locked" position (see Fig. 2).

Fig. 2

To use JAMP Clobetasol Spray follow Steps 1 through 3.

Step 1: Grip the sides of the Pump Top with one hand and use your second hand to point the Directional Spray Nozzle where you want the spray to go (see Fig. 3). The spray will be delivered through the nozzle opening at the end of the Directional Spray Nozzle.

Fig. 3

Step 2: Push down on the Pump Top to spray JAMP Clobetasol Spray (see Fig.4). In order to deliver the target dose, 6 primings would be required during the first time use.

Fig. 4

Step 3: Spray only enough to cover affected area. Rub gently to ensure even coverage. Do not apply JAMP Clobetasol Spray to your face, underarms or groin and avoid contact with eyes and lips (see Fig. 5). In case of contact, rinse thoroughly with water.

Fig. 5

4.5 Missed Dose

In the event of a missed dose, JAMP Clobetasol Spray 0.05% should be applied as soon as possible after the missed dose is remembered. If this is close to the scheduled application time for the next dose, the subject should wait and apply the next scheduled dose. The usual schedule should be resumed thereafter.

5 OVERDOSAGE

In 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 gradually under medical supervision (see **7 WARNINGS AND PRECAUTIONS**).

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Topical	Solution, 0.05% w/w	Alcohol, isopropyl myristate, sodium lauryl sulfate and undecylenic acid.

JAMP Clobetasol Spray (clobetasol propionate topical solution), 0.05% is available in 59 mL (50 g) bottles. Each gram contains 0.5 mg of clobetasol propionate. Each 59 mL bottle is accompanied by a spray pump which is to be attached by the pharmacist prior to dispensing the product. Each spray from the pump delivers approximately 0.16 mL.

7 WARNINGS AND PRECAUTIONS

General

JAMP Clobetasol Spray 0.05% should not be used under occlusive dressing, over extensive areas, or on the face, axillae, or scrotum, as sufficient absorption may occur to give rise to adrenal suppression and other systemic effects.

Clobetasol propionate belongs to the most potent class of topical corticosteroids (Class I) and prolonged use may result in serious undesirable effects (see **8.5 Post-Market**

Adverse Reactions). Treatment should not exceed 4 consecutive weeks (see 4 DOSAGE AND ADMINISTRATION).

Topical corticosteroids are known to potentially induce post-treatment rebound, relapses, development of tolerance (tachyphylaxis) and development of local or systemic toxicity such as skin atrophy, infection (including isolated cases of systemic infections), telangiectasia of the skin or hypothalamic-pituitary-adrenal axis suppression.

Endocrine and Metabolism
Clobetasol propionate is a highly potent topical corticosteroid that has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis.

Children may be more susceptible to system toxicity from use of topical corticosteroids.

Systemic absorption of topical corticosteroids has caused reversible adrenal suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

Conditions, which increase systemic absorption, include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings. Therefore, patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of adrenal suppression (see **7** Monitoring and Laboratory Tests). If adrenal suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid. Recovery of HPA axis function is generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur, requiring supplemental systemic corticosteroids. For information on systemic supplementation, see the Product Monograph for those products.

Two studies were conducted to evaluate the effect of twice daily applications of clobetasol propionate topical solution 0.05% on HPA axis function in adults with plaque psoriasis covering at least 20% of their body. Study duration was two or four weeks. In the first study, four of 14 (29%) patients displayed adrenal suppression after four weeks of use. In the second study, four of 19 (21%) of patients in the two-week treatment group and four of 17 (24%) of patients in the four-week treatment group displayed adrenal suppression. Suppression was transient, and all patients had returned to normal within 15-16 days of therapy cessation.

Hepatic/Biliary/Pancreatic
Patients with severe liver dysfunction and severe diabetes mellitus should be treated with special caution and closely monitored for side effects.

Immune
Corticosteroids have immunosuppressive properties. Topical corticosteroids may decrease resistance to infection, increase the risk of opportunistic infection and also mask some signs of infection. With increasing doses of corticosteroids, the rate of occurrence of infectious complications increases.

Cases of systemic immunosuppression and serious infections have been reported with long-term use of clobetasol propionate beyond the maximum recommended doses (see **8.5 Post-Market Adverse Reactions**). Combining clobetasol propionate with other medicines known to weaken the immune system increases the risk of systemic immunosuppression and serious infections.

Monitoring and Laboratory Tests
The following tests may be helpful in evaluating patients for HPA axis suppression:

- ACTH stimulation test
- A.M. plasma cortisol test
- Urinary free cortisol test

Musculoskeletal
Cases of osteonecrosis have been reported with long-term use of clobetasol propionate beyond the maximum recommended doses (see **8.5 Post-Market Adverse Reactions**).

Ophthalmologic
JAMP Clobetasol Spray 0.05% should not be used on plaques close to the eye because of the risk of increased intraocular pressure, glaucoma, and cataracts. Avoid any contact of the drug product with the eyes. In case of contact, the affected eye should be rinsed thoroughly with water.

Prolonged corticosteroid use may produce posterior subcapsular cataracts (especially in children), increased intraocular pressure and glaucoma with possible damage to the optic nerves, or rare diseases such as central serious chorioretinopathy (CSCR). It may also enhance secondary ocular infections due to fungi or viruses.

If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist.

Sensitivity/Resistance
Hypersensitivity to corticosteroids can be observed. JAMP Clobetasol Spray (clobetasol propionate solution) 0.05% is not recommended in patients who are hypersensitive to other corticosteroids.

If irritation develops, JAMP Clobetasol Spray 0.05% should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by a failure to heal rather than by noting a clinical exacerbation, as is the case with most products not containing a corticosteroid.

Skin
In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked generalized pustular psoriasis in case of intensive and prolonged topical use.

JAMP Clobetasol Spray 0.05% is not recommended in patient with acne vulgaris, rosacea or perioral dermatitis.

JAMP Clobetasol Spray 0.05% must not be applied on intertriginous areas (axillae and genitoanal 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.

In the presence of fungal infections, an appropriate antifungal treatment should be instituted and JAMP Clobetasol Spray 0.05% should be discontinued until the fungal infection is cured. In the presence of a bacterial infection, an appropriate antibacterial agent should be instituted. If a favorable response does not occur promptly, JAMP Clobetasol Spray 0.05% should be discontinued until the bacterial infection is adequately controlled.

7.1 Special Populations

7.1.1 Pregnant Women
There are no adequate and well-controlled studies of the teratogenic potential of clobetasol propionate in pregnant women. JAMP Clobetasol Spray 0.05% should be used during pregnancy only if its benefit justifies the potential risk to the fetus. The extent of exposure during the clinical trials with clobetasol propionate topical solution 0.05% was very limited (one case).

Corticosteroids have been shown to be teratogenic in laboratory animals when administrated systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals (see **16 NON-CLINICAL PHARMACOLOGY**).

7.1.2 Breast-feeding
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 JAMP Clobetasol Spray 0.05% is administered to a nursing woman.

Clobetasol propionate should not be prescribed to breastfeeding women unless clearly indicated.

7.1.3 Pediatrics

Safety and effectiveness of clobetasol propionate topical solution 0.05% have been established in patients 18 years and older. Insufficient data have been obtained in patients under the age of 18 years. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults for HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children.

Use in patients below 18 years of age is not recommended and is contraindicated in children below 2 years of age.

HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and an absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

7.1.4 Geriatrics

Clinical studies of clobetasol propionate topical solution 0.05% did not include sufficient numbers of patients aged 65 years and over to determine whether they respond differently than younger patients. In general, dose selection for an elderly patient should be made with caution reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

8 ADVERSE REACTIONS

8.1 Adverse Drug Reaction Overview

Systemic absorption of topical corticosteroids has produced reversible HPA axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

The following additional local adverse reactions have been reported with topical corticosteroids in general, and they may occur more frequently with the use of occlusive dressings, use over a prolonged period of time, or use over large surface areas, especially with higher potency corticosteroids, including clobetasol propionate. These reactions include: irritation, dryness, itching, burning, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, skin atrophy, atrophy of subcutaneous tissues, telangiectasia, hypertrichosis, change in pigmentation, opportunistic infection, hypersensitivity, glaucoma, striae and miliaria. If applied to the face, acne rosacea or perioral dermatitis can occur. When occlusive dressings are used, pustules, miliaria, folliculitis and pyoderma may occur. In rare instances, treatment of psoriasis with systemic or very potent topical corticosteroids (or their withdrawal) is thought to have provoked the pustular form of the disease.

Rebound effect may occur upon treatment discontinuation.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

The data presented in Table 2, below, include the combined data from two multicentre, randomized, blinded, vehicle-controlled studies conducted in patients 18 years of age or older, with moderate to severe plaque psoriasis. Clobetasol propionate topical solution 0.05% or Spray Vehicle were applied twice daily to affected areas until healing, or for a maximum of four weeks.

The most common adverse reaction reported with clobetasol propionate topical solution 0.05% is burning at the application site. Other common adverse reactions are local site effects as well, including pruritus, dryness, pain, hyperpigmentation around resolving plaque, irritation, and atrophy. Most local adverse events were rated as mild to moderate and were not affected by age, race or gender.

One serious, unexpected adverse event, designated as possibly related to treatment by the clinical investigator, was reported during the clinical trial programme with clobetasol propionate topical solution 0.05%. This severe event was reported as paranoid delusions in a subject with a seven-year history of intermittent methamphetamine use. Although the event was thought to be related to methamphetamine use by the treating psychiatrist, the possibility of a treatment relationship to clobetasol propionate solution (i.e., spray) could not be absolutely ruled out by the investigator.

Table 2 Treatment Related Adverse Events (At Least Possibly Related) Occurring at a Frequency of ≥1%of Subjects in at Least One Group (Clinical Studies TI01 - 01008 and TI01-01010 Combined)

	Clobetasol Propionate Topical Solution 0.05% n=120 (%)	Spray Vehicle n=120 (%)
General disorders and administration site conditions		
Application site atrophy	0 (0%)	1 (1%)
Application site burning	47 (39%)	55 (46%)
Application site pruritus	3 (3%)	3 (3%)
Application site dryness	2 (2%)	0 (0%)
Application site irritation	1 (1%)	0 (0%)
Application site pain	1 (1%)	2 (2%)
Application site pigmentation changes	1 (1%)	0 (0%)
Oedema peripheral	0 (0%)	1 (1%)
Sensation of pressure	0 (0%)	1 (1%)
Musculoskeletal and connective tissue disorders		
Pain in extremity	0 (0%)	1 (1%)
Skin and subcutaneous tissue disorders		
Eczema asteatotic	2 (2%)	0 (0%)
Psoriasis aggravated	0 (0%)	1 (1%)

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

One subject treated for four weeks with clobetasol propionate topical solution 0.05% experienced an elevated WBC, which was designated by the investigator as possibly related to treatment.

8.5 Post-market Adverse Reactions

The following adverse reactions have been reported in clobetasol propionate during the post-marketing setting, adrenal suppression, Cushing syndrome, glaucoma, blurred vision, hypersensitivity, allergic contact dermatitis, erythema and rash.

Cases of osteonecrosis, Kaposi's sarcoma lesions, and necrotizing fasciitis have been reported with long-term use of clobetasol propionate beyond the maximum recommended doses (see **4 DOSAGE AND ADMINISTRATION** and **7 WARNINGS AND PRECAUTIONS, Immune**).

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

The fact that clobetasol propionate could induce a six-fold induction of ethoxycoumarin- O-dealkylase activity in skin indicates that there is a potential drug-drug interaction with other topical drugs that could be metabolised by the same enzyme.

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5 Drug-Food Interactions

Interactions with food have not been established. However, given the topical route of administration, such interactions seem unlikely.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Clobetasol propionate is a super-high potency topical corticosteroid. Like other topical corticosteroids, 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 A_2 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 A_2.

10.2 Pharmacodynamics

Results of a study in healthy volunteers have shown the vasoconstriction capacity of clobetasol propionate topical solution 0.05% is comparable to that of cream formulations of clobetasol propionate and superior to that of amcinonide cream, 0.1%.

10.3 Pharmacokinetics

Absorption and

Distribution

The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle, the integrity of the epidermal barrier and the use of occlusive dressings. Topical corticosteroids can be absorbed from normal intact skin while inflammation and/or other disease processes in the skin may increase percutaneous absorption.

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids.

Metabolism and Elimination

Topical corticosteroids are metabolized, primarily in the liver, and are then excreted by the kidneys. In addition, some corticosteroids, including clobetasol propionate and its metabolites, are also excreted in the bile.

If absorbed through the skin, clobetasol propionate will be metabolized by the liver and excreted primarily via bile into the feces.

11 STORAGE, STABILITY AND DISPOSAL

Store at room temperature (15-30ºC). Do not refrigerate. Keep tightly closed. Product is flammable and should be kept away from heat or open flame. Keep in a safe place out of the reach and sight of children.

Discard 28 days after receipt from pharmacist.

12 SPECIAL HANDLING INSTRUCTIONS

There are no special handling requirements for this product.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

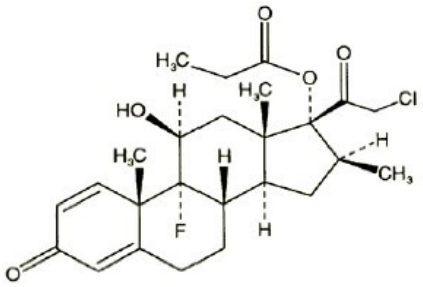
Proper name: Clobetasol propionate

Chemical name: 21-chloro-9-fluoro-11β,17-dihydroxy-16β-methylpregna-1,4- diene-3,20-dione 17-propionate

Molecular formula: $C_{25}H_{32}ClFO_5$ (CAS Registry Number 25122-46-7)

Molecular mass: 467.00 grams/mole

Structural formula:



Physicochemical properties: White to almost white crystalline powder that is Insoluble in water, freely soluble in acetone, sparingly soluble in ethanol (96%).

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

Table 3 Summary of patient demographics for clinical trials in moderate to severe plaque psoriasis

Study #	Trial design	Dosage, route of administration and duration	Study subjects (n=number)	Mean age (Range)	Gender
TI01-01008	Multicentre, randomized, double-blind, vehicle-controlled, parallel comparison	Twice daily application of a thin film to psoriatic plaques for up to four weeks	120 (60/arm)	48 (21-76)	72 M / 48 F
TI01-01010	Multicentre, randomized, double-blind, vehicle-controlled, parallel comparison	Twice daily application of a thin film to psoriatic plaques for up to four weeks	120 (60/arm)	46 (18-81)	36 M / 29 F

Two multicentre, randomized, blinded, vehicle-controlled studies were performed in patients with moderate to severe plaque psoriasis covering at least 2% of the body surface area. Patients were treated twice daily for up to four weeks with either clobetasol propionate topical solution 0.05% or Spray Vehicle.

14.2 Study Results

Efficacy assessments were based on Investigator assessments of the signs and symptoms of psoriasis. The primary measure of efficacy variable was the Overall Disease Severity score, dichotomized to success or failure. Success was defined as a Grade of 2 or less on a 0-4 point scale at Week 2 or earlier and defined as a Grade of 1 or less on a 0-4 point scale at the end of treatment (Week 4 or later).

Table 4 Results of Studies TI01-01008 and TI01-01010, separately and combined, in moderate to severe plaque psoriasis

Study No.	Primary Endpoint	Clobetasol Propionate Topical Spray 0.05%	Spray Vehicle	Statistical Significance[c]
TI01-01008	**Week 2 Overall Disease Severity[a]** Success Failure	87% 13%	28% 72%	p < 0.001
	Week 4 Overall Disease Severity[b] Success Failure	78% 22%	3% 97%	p < 0.001
TI01-01010	**Week 2 Overall Disease Severity[a]** Success Failure	87% 13%	27% 73%	p < 0.001
	Week 4 Overall Disease Severity[b] Success Failure	82% 18%	2% 98%	p < 0.001
Combined	**Week 2 Overall Disease Severity[a]** Success Failure	87% 13%	28% 72%	p < 0.001
	Week 4 Overall Disease Severity[b] Success Failure	80% 20%	3% 97%	p < 0.001

a Success is defined as a grade of 2 or less on the 0-4 point Overall Disease Severity Scale.
b Success is defined as a grade of 1 or less on the 0-4 point Overall Disease Severity Scale.
c P-value from a Cochran-Mantel-Haenszel test, stratified by grouped study sites. The Week 4 analysis is considered statistically significant if and only if statistical significance is achieved for both the Week 2 and Week 4 analyses.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

Acute Toxicity

Acute toxicity was determined in mice and rats using subcutaneous, oral, and intraperitoneal routes. The animals received a single dose of different concentrations of clobetasol propionate and were observed for three consecutive weeks. The LD_{50} value obtained by the subcutaneous route in mice was 81.7 mg/kg for all animals. None of the mice died after oral administration up to 3 g/kg. The LD_{50} value obtained by the intraperitoneal route in mice was 156 mg/kg for males and 118 mg/kg for females. The subcutaneous LD_{50} value for male rats was 397 mg/kg and 366 mg/kg for female rats.

None of the rats died after oral administration up to 3 g/kg. The LD_{50} value by the intraperitoneal route for male rats was 414 mg/kg and 351 mg/kg for female rats.

Repeated Dose Toxicity
Using clobetasol propionate topical spray 0.05%, a no observed effect dose level (NOEL) of 150 mg formulation/kg/day (safety factor of 0.9) was established for systemic toxicity in a 90-day subchronic micropig study. In a dermal toxicity study with Hanford minipigs, doses of 60, 120 and 240 mg/kg/day (safety factor 0.3, 0.65, 1.3, respectively) of clobetasol propionate topical spray 0.05% were applied for nine months followed by a one month recovery. Treatment related decreases in body weight and histopathological findings precluded the determination of a NOEL in this study.

A 90-day dermal irritation study was conducted in Sprague Dawley rats. Concentration of clobetasol propionate was varied to produce 0.001%, 0.005%, 0.015%, and 0.05% sprays. Dosing was rotated between two 20 cm^2 sites on the back and a constant volume of 0.16 mL/kg/dose (800 mg formulation/m^2/dose) was chosen based on the results a vehicle dose range finding study that found 0.24 mL/kg/dose could be tolerated in rats for 14 days. Based on the results of this study, the no-observed-adverse-effect (NOAEL) level was considered to be the 0.001% or 0.13 mg/kg (safety factor of 0.007). The effects noted during or at the end of the treatment period were reversible and most resolved almost completely by the end of a one month recovery period.

Carcinogenicity:
Few animal studies have been performed to evaluate the carcinogenic potential of isopropyl myristate and there are no detailed systemic absorption data for this compound in humans or animals.

No classical animal studies have been performed to evaluate the carcinogenic potential of clobetasol propionate.

One 18-month study was performed in mice to evaluate the carcinogenic potential of fluticasone propionate (medium-potency corticosteroid) when given topically as a 0.05% ointment. No evidence of carcinogenicity was found in this study. No evidence of pre-neoplastic lesions was noted in a 6-month toxicity study performed with clobetasol propionate by the subcutaneous route in rats.

Genotoxicity:
Clobetasol propionate was negative in the *in vivo* mammalian erythrocyte micronucleus test and in the *in vitro* mammalian chromosome aberration test conducted.

Reproductive and Developmental Toxicology:
Segment I fertility studies in rats following oral administration at doses up to 50 mcg/kg per day revealed an increase in the number of the resorbed embryos and a decrease in the number of living foetuses at the highest dose.

In another Segment I study, male rats were dosed subcutaneously twice daily beginning 70 days before cohabitation and continuing through the day before sacrifice and female rats were dosed twice daily beginning 15 days before cohabitation and continuing through Day 7 of presumed gestation. A dosage level of less than 12.5 mcg/kg/day clobetasol propionate (safety factor 0.03) was considered to be the NOEL for paternal and maternal general toxicity and male reproductive toxicity. The female reproductive NOEL was 12.5 mcg/kg/day (safety factor 0.03).

Segment II teratogenicity studies in mice, rats and rabbits showed clobetasol propionate to be teratogenic when administered subcutaneously or topically. Abnormalities seen include fetal immaturity and several malformations, cleft palate, cranioschisis and skeletal abnormalities, in combination with maternal toxicity.

A Segment II study was performed in rats using Clobetasol Propionate Lotion applied dermally at dose levels of 0.05, 0.15, and 0.5 mg/kg/day. Dose-related maternal and fetal toxicity was observed, and fetal immaturity was observed at all dose levels. A variety of fetal malformations were observed at 0.15 and 0.5 mg/kg/day, in combination with maternal toxicity.

In a Segment III study, females were dosed with clobetasol propionate suspended in 0.04% Tween® 80 in saline administered subcutaneously from Day 7 of presumed gestation through Day 20 postpartum or Day 24 presumed gestation for those rats that did not deliver a litter. The maternal NOEL for clobetasol propionate was less than 12.5 mcg/kg/day (safety factor 0.03) due to reduced body weight gain and feed consumption during the gestation period. The reproductive NOEL in the dams was 25 mcg/kg/day (safety factor 0.07). The NOAEL for viability and growth in the offspring was 12.5 mcg/kg/day (safety factor 0.03).

Local Tolerance:
Results from special toxicity studies evaluating primary dermal and ocular irritation potential showed that clobetasol propionate topical solution 0.05% is a slight skin irritant but not a skin sensitizer. It also produces moderate irritation in the Kay and Calandra Ocular Evaluation. Clobetasol propionate topical solution 0.05% is not phototoxic and does not cause photoallergy reactions.

17 SUPPORTING PRODUCT MONOGRAPHS

1. PrCLOBEX® SPRAY, Topical solution, 0.05% w/w, submission control 259690, Product Monograph, GALDERMA CANADA INC. May 12, 2022.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrJAMP Clobetasol Spray
Clobetasol Propionate Topical Solution

Read this carefully before you start using **JAMP Clobetasol Spray** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **JAMP Clobetasol Spray**.

What is JAMP Clobetasol Spray used for?
JAMP Clobetasol Spray is used in adults for the treatment of plaque type psoriasis.

How does JAMP Clobetasol Spray work?
JAMP Clobetasol Spray contains the medicinal ingredient clobetasol propionate. It belongs to a group of medicines called topical corticosteroids or topical steroids. Topical corticosteroids reduce inflammation by decreasing the body's immune response. This can relieve symptoms such as redness, scaling and itching. JAMP Clobetasol Spray is not to be used for more than 4 weeks.

What are the ingredients in JAMP Clobetasol Spray?
Medicinal ingredient: clobetasol propionate
Non-medicinal ingredients: alcohol, isopropyl myristate, sodium lauryl sulfate and undecylenic acid.

JAMP Clobetasol Spray comes in the following dosage form:
Spray, 0.05% w / w

Do not use JAMP Clobetasol Spray:
- If you are allergic to clobetasol propionate, any other corticosteroids or to any of the other ingredients in JAMP Clobetasol Spray
- If you have skin areas affected by a bacterial, mycobacterial (including tuberculosis of the skin), parasitic or fungal infection
- If you have a viral infection (such as herpes simplex, chickenpox or vaccinia)
- On wounds that have become ulcers
- In children under 2 years of age
- On or near the eyes or eyelids (risk of glaucoma or cataracts).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you use JAMP Clobetasol Spray. Talk about any health conditions or problems you may have, including if you:
- Have a weak immune response. Tell your healthcare professional if you suspect an infection has occurred as corticosteroids can make infections more likely and may mask their signs
- Have rosacea or acne

- Have plaques around your mouth, underarms, anus or genitals
- Think you have a fungal or bacterial infection. Tell your healthcare professional before you use JAMP Clobetasol Spray, because you may need other medicines to treat the infection
- Have liver problems
- Have diabetes
- Have eye problems, such as glaucoma or cataracts
- Have adrenal gland problems. JAMP Clobetasol Spray can affect how your adrenal glands work
- Use other oral or topical medication containing corticosteroids or medication intended to suppress your immune system (e.g., for autoimmune disease or after an organ transplant). Combining JAMP Clobetasol Spray with these medicines may result in serious infections
- Are less than 18 years of age. Children are at a greater risk of side effects, including adrenal suppression and may experience a decrease in the speed of their growth
- Are pregnant or trying to become pregnant
- Are breastfeeding or planning to breastfeed.

Other warnings you should know about:

- Do not use JAMP Clobetasol Spray for more than 4 weeks.
- **Adrenal Suppression:**
  - Too much JAMP Clobetasol Spray passing through your skin can shut down your adrenal glands (**adrenal suppression**). This may happen if you use too much JAMP Clobetasol Spray or if you use it for too long, but it can happen with correct use. Using JAMP Clobetasol Spray for longer than 4 weeks, over large areas of skin, on broken skin or on the face, underarms or groin can also increase your chances of developing adrenal suppression.
  - If your adrenal glands shut down, they may not start working right away after you stop using JAMP Clobetasol Spray, which will make it hard for your body to respond properly to stress or illness. It can also cause the symptoms of **Cushing's syndrome**. This is due to too much cortisol (a hormone) in your blood. It has also caused high levels of blood sugar (**hyperglycemia**) and high levels of sugar in the urine. Your healthcare professional may do special blood and urine tests to check your adrenal gland function, hormone levels and sugar levels while you are using JAMP Clobetasol Spray.
  - Covering the treated area can increase the amount of medicine absorbed through your skin. This may increase your chance of developing adrenal suppression. You should not cover the treated skin area with a bandage or other covering unless your healthcare professional tells you to.

- **Immunosuppression:** JAMP Clobetasol Spray can suppress your immune system. This may:
  - Hide symptoms of infections
  - Reactivate dormant infections
  - Cause infections due to lowered body resistance.

  Tell your healthcare professional if you suspect an infection has occurred while you

are using JAMP Clobetasol Spray.

- **Surgery:** Before you have any surgery, including at the dentist's office, tell your healthcare professional that you are using JAMP Clobetasol Spray.
- **Vision Problems:** If you experience symptoms such as increased eye pressure, blurred vision, or other visual disturbances, tell your healthcare professional. Corticosteroids, like JAMP Clobetasol Spray, can cause eye problems.
- **Allergic Contact Dermatitis:** You may develop contact dermatitis (allergic skin reaction) while using JAMP Clobetasol Spray. Tell your healthcare professional if your skin condition is not healing or gets worse.

Tell your healthcare professional about all the medicines you take and skin products you use, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

There are no known interactions with this medication.

How to use JAMP Clobetasol Spray:

- Use JAMP Clobetasol Spray only as directed by your healthcare professional in order to avoid serious side effects. Do not use more of it; do not use it more often, or for a longer period of time than your healthcare professional has told you.
- Do not use JAMP Clobetasol Spray for longer than 4 weeks. If your skin condition has not improved in 2 weeks, talk to your healthcare professional.
- As with other corticosteroids, stop using JAMP Clobetasol Spray once your plaques have healed.
- JAMP Clobetasol Spray is for external, topical use only.
- Before applying JAMP Clobetasol Spray, wash the area to be treated with a mild cleanser, pat dry, and wait several minutes.
- Do not apply JAMP Clobetasol Spray to your face, groin or armpits.
- Do not cover the treated skin area with a bandage or other covering unless your healthcare professional tells you to.
- Do not get JAMP Clobetasol Spray on or near your lips. If you get JAMP Clobetasol Spray on your lips, rinse your face with cold water right away. If you accidentally swallow JAMP Clobetasol Spray, call your regional poison control centre immediately.
- Do not use JAMP Clobetasol Spray near your eyes or eyelids (risk of glaucoma and cataracts). If you get JAMP Clobetasol Spray in your eye, flush it with cold water right away. If your eyes keep stinging after rinsing them well with water, tell your healthcare professional right away.
- JAMP Clobetasol Spray is flammable. Avoid using it near sources of heat or open flame.

Usual dose:

Adults: Apply to the affected skin areas twice daily, once in the morning and once at night. Rub in gently and completely. Use only enough to cover the affected areas. Maximum single dose: ¾ tsp or 23 sprays. Do not cover more than 20% of your body

surface area.
Maximum weekly dose: 50 mL (one bottle).

How to apply JAMP Clobetasol Spray :

Please read the following instructions before using JAMP Clobetasol Spray. The terms described in the figure below (Fig.1) will help you understand these instructions.

Fig. 1

When you receive JAMP Clobetasol Spray, the Directional Spray Nozzle is in the "locked" position (see Fig. 2).


Fig. 2

To use JAMP Clobetasol Spray follow Steps 1 through 3.

Step 1: Grip the sides of the Pump Top with one hand and use your second hand to point the Directional Spray Nozzle where you want the spray to go (see Fig. 3). The spray will be delivered through the nozzle opening at the end of the Directional Spray Nozzle.


Fig. 3

Step 2: Push down on the Pump Top to spray JAMP Clobetasol Spray (see Fig.4). In order to deliver the target dose, 6 primings would be required during the first time use.


Fig. 4

Step 3: Spray only enough to cover affected area (see Fig. 5). Rub in gently to ensure even coverage. Wash your hands after applying JAMP Clobetasol Spray.

Fig. 5

Overdose:

If you think you, or a person you are caring for, have used too much JAMP Clobetasol Spray, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed dose:

If you forget to apply JAMP Clobetasol Spray at the scheduled time, use it as soon as you remember. Then go back to your regular schedule. If it is about time for your next dose, apply just that one dose, and continue with your regular schedule the next day. Do not make up the missed dose. If you miss several doses, tell your healthcare professional.

What are possible side effects from using JAMP Clobetasol Spray ?

These are not all possible side effects you may have when using JAMP Clobetasol Spray. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- Burning, pain
- Dry skin, skin irritation
- Itching, rash, redness
- Thinning of the skin
- Swelling of the skin
- Darkening of the skin around the plaque being treated
- Inflammation and infection of the hair follicles (folliculitis)
- Spider veins
- Stretch marks
- Acne
- Excessive hair growth

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
UNCOMMON			
Adrenal suppression: Dizziness, nausea, vomiting, fever, chest pain, can lead to death			✓
Osteoporosis or Osteonecrosis (thin, fragile bones): Bone / joint pain, broken bones, back pain that gets worse when standing or walking			✓
Vision problems (glaucoma or cataracts): Failing eyesight, blurred vision, eye pain, increased pressure in your eye		✓	
Infections: Raised temperature and feeling unwell			✓
Worsening of psoriasis or Pustular psoriasis: Red, scaly, thick patches of skin, clearly defined raised bumps filled with a white, thick fluid			✓
Wounds that are slow to heal		✓	
Immunosuppression: Get sick or have infections often, purplish spots on skin or in the mouth and / or throat, swollen lymph nodes			✓
Cushing's syndrome: Weight gain in the upper body, puffy face, skin problems, hirsutism (excessive hair growth in females, acne, irregular periods), infections			✓
Hyperglycemia (high levels of sugar in the blood): Increased thirst / hunger, frequent urination, dizziness, sweating		✓	
Allergic reaction: Rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			✓
Allergic contact dermatitis: Red rash, itching, dry, scaly skin, oozing and crusting, swelling, tenderness		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store at room temperature (15-30°C). Do not refrigerate. Keep tightly closed. The spray is flammable and must be kept away from heat or flame.

Keep out of reach and sight of children.

Discard 28 days after receipt from pharmacist.

If you want more information about JAMP Clobetasol Spray:
- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (www.jamppharma.com), or by calling at 1-866-399-9091.

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