# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT
PSOCAL BETA 0.005% + 0.05% ointment

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Active substance:**
Each 1 gram ointment contains 0.0522 mg calcipotriol monohydrate equivalent to 0.05 mg calcipotriol and 0.643 mg betamethasone dipropionate equivalent to 0.5 mg betamethasone.

**Excipients:**
For a full list of excipients, see Section 6.1.

## 3. PHARMACEUTICAL FORM
Ointment
Yellowish white

## 4. CLINICAL PARTICULARS
### 4.1. Therapeutic indications
Topical treatment of stabilized psoriasis vulgaris responding to topical treatment

### 4.2. Posology and method of administration
**Posology/Frequency and duration of administration:**
PSOCAL BETA is applied to the affected area once daily. The recommended treatment period is 4 weeks. There is experience with repeated courses of PSOCAL BETA up to 52 weeks. If it is necessary to continue or restart treatment after 4 weeks, treatment should be continued after medical review and under regular medical supervision.

When using calcipotriol containing medicinal products, the maximum daily dose should not exceed 15 grams and the maximum weekly dose should not exceed 100 grams. The body surface area treated should not exceed 30% of the total body surface (see Section 4.4).

**Method of Administration:**
PSOCAL BETA is applied to the affected area and rub until absorbed. In order to achieve optimal effect, it is recommended not to take a shower or bath immediately after application of PSOCAL BETA.
It should not be applied to face skin and genital area.
Ointment can be preferably administered in the evening.

As PSOCAL BETA is an oily product, do not wear it immediately after applying.

**Additional information about special populations**
**Renal/Hepatic Failure:**
It should not be used in patients with severe renal failure or severe liver disease.

**Pediatric population:**
PSOCAL BETA is not recommended for use in children and adolescents under 18 years of age. PSOCAL BETA has not been evaluated for safety and efficacy in children under 18

years of age. Currently available data in children aged 12 to 17 years are described in section 4.8 and 5.1 but no recommendation on a posology can be made. Its use is not recommended in the childhood age group unless it is mandatory.

**4.3. Contraindications**

It is contraindicated in patients with known hypersensitivity to any of the ingredients in its composition.

Since PSOCAL BETA contains calcipotriol, it is contraindicated in patients known disorders of calcium metabolism (see Section 4.4).

In addition, since PSOCAL BETA contains corticosteroids, it is contraindicated in the following cases: viral (e.g. herpes or varicella) lesions of the skin, fungal or bacterial skin infections, parasitic infections, skin manifestations in relation to tuberculosis, rosacea, perioral dermatitis, acne vulgaris, atrophic skin, striae atrophicae, fragility of skin veins, ichthyosis, acne rosacea, ulcers, wound-related skin lesions.

PSOCAL BETA is contraindicated in erythrodermic, exfoliative and pustular psoriasis.

**4.4. Special warnings and precautions for use**

Effects on endocrine system

Adverse reactions found in connection with systemic corticosteroid treatment, such as adrenocortical suppression or impact on the metabolic control of diabetes mellitus may occur also during topical corticosteroid treatment due to systemic absorption.

Application under occlusive dressings, on large areas of damaged skin or on mucous membranes or in skin folds should be avoided since it increases the systemic absorption of corticosteroids (see Section 4.8).

In a study in patients with both extensive scalp and body psoriasis using a combination of high doses of gel form containing the same active ingredients as the PSOCAL BETA ointment applied to the body and applying to the scalp, 5 of 32 patients showed a borderline decrease in cortisol response to adrenocorticotropic hormone (ACTH) after 4 weeks of treatment (see section 5.1).

Effects on calcium metabolism

Due to the content of calcipotriol, hypercalcaemia may occur if the maximum weekly dose (100 g) is exceeded. Serum calcium is normalised when treatment is discontinued. The risk of hypercalcaemia is minimal when the recommendations relevant to calcipotriol are followed.

Local adverse reactions

PSOCAL BETA contains a potent group III-steroid and concurrent treatment with other steroids on the same treatment area must be avoided.

Skin of the face and genitals are very sensitive to corticosteroids. The medicinal product should not be used in these areas.

The patient must be instructed in correct use of the medicinal product to avoid application and accidental transfer to the face, mouth and eyes. Hands must be washed after each application to avoid accidental transfer to these areas.

Concomitant skin infections
When lesions become secondarily infected, they should be treated with antimicrobiological therapy. However, if infection worsens, treatment with corticosteroids should be stopped (see section 4.3).

Discontinuation of treatment
When treating psoriasis with topical corticosteroids there may be a risk of generalised pustular psoriasis or of rebound effects when discontinuing treatment. Medical supervision should therefore continue in the post-treatment period.

Long-term use
With long-term use there is an increased risk of local and systemic corticosteroid adverse reactions. The treatment should be discontinued in case of adverse reactions related to long-term use of corticosteroid (see section 4.8).

Unevaluated uses
There is no experience with the use of PSOCAL BETA in guttate psoriasis.

Concurrent treatment and UV exposure
PSOCAL BETA for body psoriasis lesions has been used in combination with gel form which is used for scalp psoriasis lesions and contains same active ingredients but there is limited experience of combination of PSOCAL BETA with other topical anti-psoriatic products at the same treatment area, other anti-psoriatic medicinal products administered systemically or with phototherapy.

During PSOCAL BETA treatment, physicians are recommended to advise patients to limit or avoid excessive exposure to either natural or artificial sunlight. Topical calcipotriol should be used with UV radiation only if the physician and patient consider that the potential benefits outweigh the potential risks (see section 5.3).

Butyl hydroxy toluene (E321) present in the polyoxypropylene-11-stearyl ether excipient of PSOCAL BETA may cause local skin reactions (e.g. contact dermatitis) or irritation of the eyes and mucous membranes.

**4.5. Interactions with other medicinal products and other forms of interactions**
There are no known interactions.

**4.6. Pregnancy and lactation**
**General recommendation:**
Pregnancy category C

**Women with childbearing potential / Birth control (Contraception):**
There are no adequate data from the use of PSOCAL BETA in pregnant women.

**Pregnancy:**
There are no adequate data from the use of PSOCAL BETA in pregnant women. Studies in animals with glucocorticoids have shown reproductive toxicity (see section 5.3), but a number of epidemiological studies (less than 300 pregnancy outcomes) have not revealed congenital anomalies among infants born to women treated with corticosteroids during pregnancy. The

potential risk for humans is uncertain. Therefore, during pregnancy, PSOCAL BETA should only be used when the potential benefit justifies the potential risk.

**Lactation:**
Betamethasone passes into breast milk but risk of an adverse effect on the infant seems unlikely with therapeutic doses. There are no data on the excretion of calcipotriol in breast milk. Caution should be exercised when prescribing PSOCAL BETA to women who breast-feed. The patient should be instructed not to use PSOCAL BETA on the breast when breast-feeding.

**Reproduction/Fertility:**
Studies in rats with oral doses of calcipotriol or betamethasone dipropionate demonstrated no impairment of male and female fertility (see section 5.3).

**4.7. Effects on ability to drive and use of machines**
PSOCAL BETA has no or negligible influence on the ability to drive and to use machines.

**4.8. Undesirable effects**
The estimation of the frequency of adverse reactions is based on a pooled analysis of data from clinical studies including post-authorisation safety studies and spontaneous reporting.

The most frequently reported adverse reactions during treatment are various skin reactions, like pruritus and skin exfoliations.

Adverse reactions are listed by MedDRA SOC and the individual adverse reactions are listed starting with the most frequently reported. Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness. Frequencies are defined as follows: Very common (≥1 / 10); common (≥1 / 100 to <1/10); uncommon (≥1 / 1000) to <1/100); rare (≥1 / 10,000 to <1/1000); very rare (<1 / 10,000), unknown (can not be estimated from the available data).

**Infections and infestations**
Uncommon:
Skin infection *, folliculitis

Rare:
Furuncle

**Immune system diseases**
Rare:
Hypersensitivity

**Metabolism and nutritional diseases**
Rare:
Hypercalcemia

**Skin and subcutaneous tissue diseases**
Common:
Skin exfoliation, itching

Uncommon:
Atrophic skin, exacerbation of psoriasis, dermatitis, erythema, rash **, purpura or ecchymosis, skin burning sensation, skin irritation

Rare:
Pustular psoriasis, skin striae, photosensitivity reactions, acne, dry skin

**General disorders and administration site conditions**
Uncommon:
Application site pigmentation changes, application site pain ***

Rare:
Rebound effect

*Skin infections including bacterial, fungal and viral skin infections have been reported.
**Various types of rash reactions such as exfoliative rash, rash popular and rash pustular have been reported.
***Application site burning is included in application site pain

**Additional information about special populations**
**Pediatric population:**
In an uncontrolled open study, 33 adolescents aged 12-17 years with psoriasis vulgaris were treated with PSOCAL BETA for 4 weeks to a maximum of 56 g per week. No new adverse events were observed and no concerns regarding systemic corticosteroid effect were identified. The size of this study does however not allow firm conclusions regarding the safety profile of PSOCAL BETA in children and adolescents.

The following adverse reactions are considered to be related to the pharmacological classes of calcipotriol and betamethasone, respectively:

- Calcipotriol

Adverse reactions include application site reactions, pruritus, skin irritation, burning and stinging sensation, dry skin, erythema, rash, dermatitis, eczema, psoriasis aggravated, photosensitivity and hypersensitivity reactions including very rare cases of angioedema and facial oedema.

Systemic effects after topical use may appear very rarely causing hypercalcaemia or hypercalciuria (see section 4.4).

- Betamethasone (as dipropionate)

PSOCAL BETA contains a potent corticosteroid.
Local reactions can occur after topical use, especially during prolonged application, including skin atrophy, telangiectasia, striae, folliculitis, hypertrichosis, perioral dermatitis, allergic contact dermatitis, depigmentation and colloid milia.

When treating psoriasis with topical corticosteroids there may be a risk of generalised pustular psoriasis.

Systemic reactions due to topical use of corticosteroids are rare in adults, however they can be severe. Adrenocortical suppression, cataract, infections, impact on the metabolic control of diabetes mellitus and increase of intra-ocular pressure can occur, especially after long term treatment. Systemic reactions occur more frequently when applied under occlusion (plastic, skin folds), when applied on large areas and during long term treatment (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 Turkish Pharmacovigilance Center (TÜFAM). (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; tel.: 800 314 00 08; fax: 0 312 218 35 99)

**4.9. Overdose**
Use above the recommended dose may cause elevated serum calcium which subsides when treatment is discontinued. The symptoms of hypercalcaemia include polyuria, constipation, muscle weakness, confusion and coma.

Excessive prolonged use of topical corticosteroids may suppress the pituitary-adrenal functions resulting in secondary adrenal insufficiency which is usually reversible. In such cases symptomatic treatment is indicated.

In case of chronic toxicity the corticosteroid treatment must be discontinued gradually.

It has been reported that due to misuse one patient with extensive erythrodermic psoriasis treated with 240 g of PSOCAL BETA weekly (corresponding to a daily dose of approximately 34 g) for 5 months (maximum recommended dose 15 g daily) developed Cushing's syndrome during treatment and then pustular psoriasis after abruptly stopping treatment.

**5. PHARMACOLOGICAL PROPERTIES**
**5.1. Pharmacodynamic properties**
**Pharmacotherapeutic group**: Other antipsoriatics for topical use
**ATC Code**: D05AX52 calcipotriol combinations

In vitro data suggests that calcipotriol which is a vitamin D derivative induces differentiation and suppresses proliferation of keratocytes. This is the proposed basis for its effect in psoriasis.

Like other topical corticosteroids, betamethasone dipropionate has anti-inflammatory, antipruritic, vasoconstrictive and immunosuppresive properties, however, without curing the underlying condition. Through occlusion the effect can be enhanced due to increased penetration of the stratum corneum (about 10 times). The adverse events will increase because of this. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear.

A safety study in 634 psoriasis patients has investigated repeated courses of PSOCAL BETA used once daily as required, either alone or alternating with calcipotriol containing ointment, for up to 52 weeks, compared with only calcipotriol containing ointment used for 48 weeks after an initial course of PSOCAL BETA. Adverse drug reactions were reported by 21.7 % of

the patients in the PSOCAL BETA group, 29.6 % in the PSOCAL BETA/calcipotriol ointment alternating group and 37.9 % in the calcipotriol group. The adverse drug reactions that were reported by more than 2 % of the patients in the PSOCAL BETA group were pruritus (5.8 %) (e.g. skin atrophy, folliculitis, depigmentation, furuncle and purpura) and psoriasis (5.3 %). Adverse events of concern possibly related to long-term corticosteroid use were reported by 4.8 % of the patients in the PSOCAL BETA group, 2.8 % in the PSOCAL BETA /calcipotriol alternating group and 2.9 % in the calcipotriol group.

Adrenal response to ACTH was determined by measuring serum cortisol levels in patients with both extensive scalp and body psoriasis, using combinations of PSOCAL BETA up to 106 g once a week and gel form containing the same active ingredients as PSOCAL BETA. A borderline decrease in cortisol response at 30 minutes post ACTH exposure was seen in 5 of 32 patients (15.6 %) after 4 weeks of treatment and in 2 of 11 patients (18.2 %) who continued treatment until 8 weeks. In all cases, the serum cortisol levels were normal at 60 minutes post ACTH exposure. There was no evidence of change of calcium metabolism observed in these patients. With regard to Hypothalamus-Pituitary-Adrenal (HPA) suppression, therefore, this study shows some evidence that very high doses of gel form containing the same active ingredients as PSOCAL BETA and PSOCAL BETA may have a weak effect on the HPA axis.

Paediatric population
The adrenal response to ACTH exposure was measured in an uncontrolled 4-week study in 33 adolescents aged 12-17 years with body psoriasis who used up to 56 g per week of PSOCAL BETA. No cases of HPA axis suppression were reported. No hypercalcaemia was reported but one patient had a possible treatment related increase in urinary calcium.

**5.2. Pharmacokinetic properties:**
**General properties**
Absorption:
Clinical studies with radiolabelled ointment indicate that the systemic absorption of calcipotriol and betamethasone from PSOCAL BETA is less than 1 % of the dose (2.5 g) when applied to normal skin (625 cm2) for 12 hours. Application to psoriasis plaques and under occlusive dressings may increase the absorption of topical corticosteroids. Absorption through damaged skin is approx. 24 %.

Calcipotriol and betamethasone dipropionate were below the lower limit of quantification in all blood samples of 34 patients treated for 4 or 8 weeks with gel form containing same active ingredients as PSOCAL BETA and PSOCAL BETA for extensive psoriasis involving the body and scalp. One metabolite of calcipotriol and one metabolite of betamethasone dipropionate were quantifiable in some of the patients.

Distribution:
Protein binding is approx. 64 %. In rats, tissue distribution studies with radiolabelled calcipotriol and betamethasone dipropionate, respectively, showed that the kidney and liver had the highest level of radioactivity.

Biotransformation:
Following systemic exposure, both active ingredients – calcipotriol and betamethasone dipropionate – are rapidly and extensively metabolised. Betamethasone is metabolised especially in the liver, but also in the kidneys to glucuronide and sulfate esters.

Elimination:
Plasma elimination half-life after intravenous application is 5-6 hours. Due to the formation of a depot in the skin, elimination after dermal application is in order of days. The main route of excretion of calcipotriol is via faeces (rats and minipigs) and for betamethasone dipropionate it is via urine (rats and mice).

**5.3. Preclinical safety data**
Studies of corticosteroids in animals have shown reproductive toxicity (cleft palate, skeletal malformations). In reproduction toxicity studies with long-term oral administration of corticosteroids to rats, prolonged gestation and prolonged and difficult labour were detected. Moreover, reduction in offspring survival, weight loss and weight gain was observed. There was no impairment of fertility. The relevance for humans is unknown.

A dermal carcinogenicity study with calcipotriol in mice and an oral carcinogenicity study in rats revealed no special risk to humans.

Photo(co)carcinogenicity studies in mice suggest that calcipotriol may enhance the effect of UV radiation to induce skin tumours.

A dermal carcinogenicity study in mice and an oral carcinogenicity study in rats revealed no special risk of betamethasone dipropionate to humans. No photocarcinogenicity study has been performed with betamethasone dipropionate.

**6. PHARMACEUTICAL PARTICULARS**
**6.1. List of excipients**
Liquid paraffin
Polyoxypropylene-11-stearyl ether (including butyl hydroxy toluene (E321))
Vitamin E (α-tocopherol)
White soft paraffin

**6.2. Incompatibilities**
Not applicable.

**6.3. Shelf life**
24 months if the tube is not opened. 12 months after first opening of the tube.

**6.4. Special precautions for storage**
Store it at room temperature below 25°C.

**6.5. Nature and contents of container**
30 gram aluminum tube with HDPE cover.

**6.6. Special precautions for disposal and other handling**
Any unused product or waste material should be disposed of in accordance with “Directive on Control of Medical Waste” and “Directive on the Control of Packaging and Packaging Waste.

**7. MARKETING AUTHORIZATION HOLDER**

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**8. MARKETING AUTHORIZATION NUMBER(S)**

2017/888

**9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION**

Date of the first authorization: 24.11.2017
MA renewal date:

**10. DATE OF REVISION OF THE TEXT**

19.04.2021