13 Part VI: Summary of activities in the risk management plan by product

13.1 Part VI.1 Elements for summary tables in the EPAR

Table 13-1 Part VI.1.1 Summary table of safety concerns

Important identified risks	Hypercalcaemia
	HPA axis suppression
	Skin atrophy
Important potential risks	Potential enhancement of UV radiation induced skin cancer
Missing information	None

Table 13-2 Part VI.1.2 Table of on-going and planned studies/ activities in the Post-authorization Pharmacovigilance Development Plan

N/A

Table 13-3 Part VI.1.3 Summary of Post authorization efficacy development plan

N/A

Table 13-4 Part VI.1.4 Summary table of risk minimization measures

Safety concern	Routine risk minimization measures	Additional risk minimization measures
Hypercalcaemia	Guidance is provided in sections 4.4 Special warnings and precautions for use and 4.8 Undesirable effects of the SmPC.	None
HPA axis suppression	Guidance is provided in sections 5.1 Pharmacodynamic properties of the SmPC.	None
Skin atrophy	Guidance is provided in sections 4.4 Special warnings and precautions for use and 4.8 Undesirable effects of the SmPC	None
Potential enhancement of UV radiation induced skin cancer	Guidance is provided in sections 4.4 Special warnings and precautions for use and 5.3 Preclinical safety data of the SmPC.	None

13.2 Part VI.2 Elements for a Public Summary

13.2.1 Part VI.2.1 Overview of disease epidemiology

Plaque psoriasis vulgaris is a disease causing red, scaly patches on the skin. Men and women are equally affected. It can occur at any age but the majority of cases first present before the age of 35 years but it is uncommon in children. The number of affected children ranges from 0% (Taiwan) to 2.1% (Italy), and in adults it varies from 0.91% (United States) to 8.5% (Norway) [Parisi R, 2013] . With four out of five (or 80% of) people with psoriasis having plaque psoriasis, plaque psoriasis is the most common form of psoriasis. Plaque psoriasis can

appear anywhere on the body, but often pops up in the areas of the elbows, knees, scalp and lower back.

13.2.2 Part VI.2.2 Summary of treatment benefits

There are several standard medications for the treatment of psoriasis, e.g. topical treatments (applied on the skin) like Betamethasone/ Calcipotriol ointment, Vitamin D analogues, retinoids, moreover light therapy (phototherapy) or oral/ injected medications like cyclosporine or immunomodulator drugs (biologics).

Betamethasone/ Calcipotriol ointment contains two active substances: calcipotriol and betamethasone. Calcipotriol, a substance derived from vitamin D, acts through receptors in the skin to prevent the multiplication of cells that cause the scaly patches in psoriasis. Betamethasone is an anti-inflammatory medicine that helps to reduce the inflammation and itching that occur with psoriasis.

13.2.3 Part VI.2.3 Unknowns relating to treatment benefits

There are no adequate data from the use of Betamethasone/ Calcipotriol in children below the age of 18 years and in pregnant and breast-feeding women. Moreover the safety and efficacy of Betamethasone/ Calcipotriol ointment in patients with guttate psoriasis, severe renal insufficiency or severe hepatic disorders have not been evaluated. There is no experience of combination of Betamethasone/ Calcipotriol with other topical anti-psoriatic products at the same treatment area or other anti-psoriatic medicinal products administered systemically.

13.2.4 Part VI.2.4 Summary of safety concerns

Table 13-5 Important identified risks

Risk	What is known	Preventability
Increased blood level of calcium (Hypercalcaemia)	Due to the content of calcipotriol, hypercalcaemia may occur if the maximum daily dose (15 g) is exceeded. Serum calcium is, however, quickly normalised when treatment is discontinued.	The risk of hypercalcaemia is minimal when the recommendations relevant to calcipotriol are followed.
Side effects due to suppression of complex feedback interactions among three endocrine glands: the hypothalamus, the pituitary gland (a pea-shaped structure located below the hypothalamus), and the adrenal (also called "suprarenal") glands (small, conical organs on top of the kidneys) (HPA axis suppression)	Systemic absorption of topical corticosteriods can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression. Clinical apparent and serious symptoms are.	Patients applying a topical steroid to a large surface area or areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. The risk of serious adverse reactions can be mitigated by monitoring for early symptoms.
Shrinking and thinning of skin (Skin atrophy)	Thinning of the skin may affect up to 1 in 100 patients using Betamethasone/ Calcipotriol ointment. Local reactions can	In such cases, symptomatic treatment is indicated. In case of chronic toxicity, the corticosteroid treatment must be

Risk	What is known	Preventability
	occur after topical use, especially during prolonged application.	discontinued gradually.

Table 13-6 Important potential risks

Risk	What is known
Enhanced effect of UV radiation (UVR) to induce skin cancer	Studies in mice suggest that calcipotriol may enhance the effect of UVR to induce skin cancer. During Betamethasone/ Calcipotriol 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 UVR only if the physician and patient consider that the potential benefits outweigh the potential risks.

Table 13-7 Missing information

None

13.2.5 Part VI.2.5 Summary of additional risk minimization measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimizing them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures

13.2.6 Part VI.2.6 Planned post authorization development plan

None.

13.2.7 Part VI.2.7 Summary of changes to the Risk Management Plan over time

N/A