

## **VI.2 Elements for a Public Summary**

### **VI.2.1 Overview of disease epidemiology**

#### **Psoriasis (excluding widespread plaque psoriasis)**

Psoriasis is a common chronic skin disorder. Estimates of the prevalence (proportion of individuals in a population having this disease) of psoriasis have varied across studies. A systematic review found wide variation in the global prevalence of psoriasis. The prevalence of psoriasis in adults ranged from 0.91 to 8.5 percent, and the prevalence of the disease in children ranged from 0 to 2.1 percent. Geographic location appeared to influence the likelihood of having psoriasis; disease prevalence tended to increase with increasing distance from the equator. Furthermore, there is no clear gender predilection for psoriasis. Although psoriasis can begin at any age, the disease is less common in children than adults. There seem to be two peaks for the age of onset which differ slightly between the genders: females experience onset more frequently between the ages of 20-29 and 50-59, whereas men experience onset more frequently between the ages of 30-39 and 60-79<sup>1</sup>.

#### **Recalcitrant eczema**

Atopic eczema is a chronic, relapsing, inflammatory skin condition characterised by an itchy red rash that favours the skin creases such as the folds of the elbows or behind the knees. Atopic eczema is common and the prevalence is increasing. In this context, a population based study in USA reported that eczema (defined as itching/scratching and red/inflamed rash or excessive dryness/scaling) was present in 10.7% of the population<sup>5</sup>.

#### **Lichen planus**

Lichen planus is a skin disease that mainly affects the skin to cause an itchy rash. In some cases it affects the mouth, genitals, hair, nails and (rarely) other parts of the body. While it may occur at any age, it usually occurs in adults aged 30-60 years and it is reported in approximately 1% of all new patients seen at health care clinics<sup>7</sup>.

#### **Discoid lupus erythematosus**

Discoid lupus erythematosus (DLE) is a chronic photosensitive skin eruption which can be either localised or widespread and classically presents with red to violet coloured scaly plaques with blocked follicles that often results in scarring and atrophy. DLE is responsible for 50-85% of cases of chronic lupus erythematosus and occurs 2-3 times more frequently in women than in men. Although DLE may occur at any age, it most often develops in persons aged 20-40 years<sup>9</sup>.

### **VI.2.2 Summary of treatment benefits**

#### **Psoriasis**

Clobetasol propionate cream has been compared with control lotion for the treatment of psoriasis in three different investigations and all studies demonstrate that clobetasol propionate was more efficient than the control. Furthermore, in another study comparing the efficacy of clobetasol propionate cream

and tazarotene (topical treatment for psoriasis) against palmoplantar psoriasis, it was reported that both therapies improved the outcome.

**Recalcitrant dermatoses**

In a review article, it is concluded that clobetasol propionate is useful for short-term intensive treatment of eczema. Furthermore, the efficacy of clobetasol propionate or control lotion was evaluated in 81 patients suffering from atopic dermatitis. Clobetasol propionate was more effective than control against e.g. erythema, pruritus (itching), size/dryness and the improvement of the lesions was maintained throughout the treatment period.

**Lichen planus**

A study including 30 patients was conducted to compare clobetasol and tacrolimus (an immunosuppressive drug) in the topical management of oral lichen planus. The study found that clobetasol was as useful as tacrolimus<sup>10</sup>. In another investigation, two different doses of clobetasol propionate were evaluated in patients suffering from oral lichen planus. Clinical improvement was reported in the majority of the patients in both groups and no difference was detected between the groups.

**Discoid lupus erythematosus**

The efficacy and safety of topical tacrolimus and clobetasol propionate were evaluated in 20 patients suffering from lupus erythematosus and both therapies were effective in treating lupus erythematosus.

**VI.2.3 Unknowns relating to treatment benefits**

There are limited data from the use of clobetasol propionate in pregnant women and during breastfeeding

**VI.2.4 Summary of safety concerns**

**Important identified risks**

Risk	What is known	Preventability
Cushing syndrome and hypothalamic-pituitary adrenal axis suppression	If Closol is used in large quantities, for a prolonged time period or if a large area is treated, the product may be absorbed through the skin and into the blood stream and result in high levels of cortisol systemically (Cushing’s syndrome). This side effect is most likely to occur in children and infants or if an occlusion is used. Prolonged treatment may also cause adrenocortical suppression, which means that the body produces lower levels of the hormone cortisol than normal. This may in turn result in delayed growth and weight gain in children, hair loss, hypertension, osteoporosis,	Do not use large quantities of Closol for a prolonged period. Only use Closol for as long as your doctor recommends. If your condition does not improve with 4 weeks of treatment, speak to your doctor.  Do not use Closol in children under the age of 1.  Only use an occlusive dressing over Closol if your doctor has told you to.

Risk	What is known	Preventability
	glaucoma, cataract, blood glucose increase.	
Hypersensitivity	Clobetasol propionate or any of the excipients in Closol may cause allergic reactions.	<p>Tell your doctor before starting treatment if you are allergic (hypersensitive) to Closol or any of the other ingredients of the product.</p> <p>Stop using Closol immediately and tell your doctor if you develop an allergic reaction.</p>
Eye disorders, including cataract and glaucoma	When applying Closol onto the eyelid the product may come into the eye and thereby, there is a risk of developing glaucoma (clouding of the lens).	Avoid getting Closol in the eye and rinse thoroughly with water if necessary.
Telangiectasia	Closol can cause telangiectasia, also known as spider veins. This is a condition of small dilated blood vessels near the surface of the skin or the mucous membranes. Telangiectasia is a symptom of Cushing's syndrome.	<p>Do not use large quantities of Closol for a prolonged period. Only use Closol for as long as your doctor recommends. If your condition does not improve with 4 weeks of treatment, speak to your doctor.</p> <p>Do not use Closol in children under the age of 1.</p> <p>Only use an occlusive dressing over Closol if your doctor has told you to.</p>
Immunosuppression and opportunistic infections	<p><b>Infections</b> Prolonged treatment with Closol can cause adrenocortical suppression. This can lead to impairment of the immune system so that you will be more prone to infections.</p> <p><b>Occlusive dressings</b> Bacterial infection is stimulated by the warm, moist conditions within e.g. skin folds or caused by occlusive dressings.</p>	<p>Do not use large quantities of Closol for a prolonged period. Only use Closol for as long as your doctor recommends. If your condition does not improve with 4 weeks of treatment, speak to your doctor.</p> <p>Do not use Closol in children under the age of 1. Only use an occlusive dressing over Closol if your doctor has told you to.</p> <p><b>Occlusive dressings</b> Tell your doctor if you find that the area being treated becomes infected and stop Closol treatment if the infection spreads and begin proper treatment.</p> <p>Only use an occlusive dressing over Closol if your doctor has told you to. If you are applying</p>

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
		<p>Closol under an occlusive dressing, make sure that the skin is cleansed before a dressing is applied to prevent infections.</p> <p>Do not use Closol onto open wounds or if you suffer from a fungi, bacterial or viral infection.</p>
Skin atrophy and pigmentation changes	Closol cause changes in skin colour and skin thinning.	Only use Closol for as long as your doctor recommends. If your condition has not improved within 2 – 4 weeks of treatment, speak to your doctor.
Exacerbation of the skin condition	In some cases of psoriasis, treatment with Closol has worsened the skin condition.	If your condition worsens when using Closol. Speak to your doctor.
Rebound phenomenon of the skin condition upon abrupt discontinuation	Abrupt discontinuation of treatment after prolonged use may cause reddening and pain of the skin and psoriasis can be worsened.	When Closol has been used for a long-time period, treatment should be gradually phased out. This can be done by applying Closol less frequently or by using a product that is less concentrated.
Growth retardation	Children are more prone to develop adverse reactions from the use of topical corticosteroids such as Closol. Growth retardation in children can occur after prolonged use.	<p>Do not use large quantities of Closol for a prolonged period. Only use Closol for as long as your doctor recommends. If the condition does not improve with 4 weeks of treatment, speak to your doctor.</p> <p>Do not use Closol in children under the age of 1.</p> <p>Only use an occlusive dressing over Closol if your doctor has told you to.</p>

### **Important potential risks**

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
Off label use	Closol may be used for treatment of other conditions than the intended.	<p>The doctor's instructions should be followed carefully. In case of questions contact the doctor or pharmacy.</p> <p>Do not use large quantities of Closol for a prolonged period. Only use Closol for as long as your doctor recommends. If the condition does not improve with 4 weeks of treatment, speak to your doctor.</p>

Risk	What is known	Preventability
		<p>Do not use Closol in children under the age of 1.</p> <p>Only use an occlusive dressing over Closol if your doctor has told you to.</p>
Misuse for prolonged duration	<p>If Closol is used for a prolonged time period, the product may be absorbed through the skin and into the blood stream and result in high levels of cortisol systemically. This can lead to several adverse reactions such as Cushing's syndrome, adrenocortical suppression, delayed growth and weight gain in children, hair loss, hypertension, osteoporosis, glaucoma, cataract, and blood glucose increase.</p>	<p>Do not use large quantities of Closol for a prolonged period. Only use Closol for as long as your doctor recommends. If your condition does not improve with 4 weeks of treatment, speak to your doctor.</p>
Diabetes and impairment of adequate glucose control	<p>If Closol is used for a prolonged time period, the product may be absorbed through the skin and into the blood stream and result in high levels of cortisol systemically. This can lead to increased blood glucose.</p>	<p>Do not use large quantities of Closol for a prolonged period. Only use Closol for as long as your doctor recommends. If your condition does not improve with 4 weeks of treatment, speak to your doctor.</p> <p>Frequent urination, thirst and tiredness may be signs of increased blood glucose. Contact your doctor.</p>
Vascular disorders, other than telangiectasia	<p>If Closol is used for a prolonged time period, the product may be absorbed through the skin and into the blood stream and result in high levels of cortisol systemically. This can lead to increased blood pressure.</p>	<p>Do not use large quantities of Closol for a prolonged period. Only use Closol for as long as your doctor recommends. If your condition does not improve with 4 weeks of treatment, speak to your doctor.</p> <p>In case of increased blood pressure, contact your doctor.</p>
Intracranial hypertension	<p>Increased intracranial blood pressure is a rare adverse reaction that may develop when you stop using Closol. The reaction can develop after sudden stopping the medication after long-time use.</p>	<p>Do not use large quantities of Closol for a prolonged period. Only use Closol for as long as your doctor recommends. If your condition does not improve with 4 weeks of treatment, speak to your doctor.</p> <p>When Closol has been used for a long-time period, treatment should be gradually phased out. This can be done by applying</p>

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
		Closol less frequently or by using a product that is less concentrated.

### **Missing information**

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
Use during pregnancy and lactation	The use of topical corticosteroids such as Closol may affect the growth of the fetus if you are pregnant. However, little is known about this risk. Breastfeeding will probably not affect the baby if you are using Closol.	If you are breastfeeding, or pregnant, or suspect that you are pregnant, you should contact your doctor or the pharmacy before using Closol.

#### **VI.2.5 Summary of risk minimisation 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 minimising 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.

The summary of product characteristics and package leaflet for Closol hard capsules can be found in the national competent authority's website.

This medicine has no additional risk minimisation measures.

#### **Safety concern in lay terms (medical term)**

Not applicable

#### **VI.2.6 Planned post authorisation development plan**

Not applicable

#### **VI.2.7 Summary of changes to the Risk Management Plan over time**

Not applicable, this is the first RMP