

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

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

Bemeson is intended for the treatment of:

Atopic dermatitis

Nummular dermatitis (discoïd eczema).

Prurigo nodularis.

Psoriasis (excluding widespread plaque psoriasis).

Lichen simplex chronicus (neurodermatit) and lichen planus.

Seborrhoeic dermatitis.

Irritable or allergic contact dermatitis.

Discoïd lupus erythematosus.

Addendum to systemic steroid therapy in generalized erythroderma.

Reactions to insect bites.

Miliaria (prickly heat).

#### **Atopic dermatitis**

Atopic dermatitis (AD) is a chronic, highly pruritic (itchy) inflammatory skin disease and one of the most common skin disorders in children and the prevalence (proportion of individuals in a population having this disease) of AD has increased over the past 30 years. It is currently estimated that 10% of children and 0.9% of adults in developed countries are affected by the disorder. AD often starts in early infancy; 85% of the cases occur during the first year of life and 95% before 5 years of age<sup>2,3</sup>.

#### **Nummular dermatitis (discoïd eczema)**

Nummular (meaning "coin-shaped") dermatitis is a form of eczema. The prevalence of nummular dermatitis is 2 cases per 1000 people and it is uncommon in children. Nummular dermatitis is more common in males than in females<sup>6</sup>.

#### **Dyshidrotic eczema**

Dyshidrotic eczema is a type of eczema that is characterized by a pruritic vesicular eruption on the fingers, palms, and soles and may be triggered by sensitivity to e.g. nickel, ingested metals or bacterial infection. The condition affects teenagers and adults and may be acute, recurrent, or chronic. In a study of 107,206 Swedish individuals, 51 (0.05%) were diagnosed with dyshidrosis. Of all hand

dermatitis cases in that population, 3% had dyshidrosis. In a study reviewing records of 714 Portuguese patients during a 6-year period was found dyshidrotic eczema to be the third most common type of hand dermatitis (20.3%). Dyshidrotic eczema affects individuals aged 4-76 years; the mean age is 38 years<sup>8</sup>.

### **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>9</sup>.

### **Lichen simplex chronicus (neurodermatitis) and lichen planus**

Lichen simplex chronicus (LSC) is thickening of the skin with variable scaling that arises secondary to repetitive scratching or rubbing. Exact frequency in the general population is unknown. In one study, 12% of aging patients with pruritic skin had LSC. LSC is observed more commonly in females than in males and occurs mostly in mid-to-late adulthood, with highest prevalence in persons aged 30-50 years<sup>12</sup>.

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>13</sup>.

### **Seborrheic dermatitis**

Seborrheic dermatitis is a chronic, relapsing, and usually mild form of dermatitis. The usual onset occurs with puberty and then it peaks at the age of 40, but is present among older people as well. The prevalence rate of seborrheic dermatitis is 3-5% with a worldwide distribution. Dandruff, the mildest form of this dermatitis, is probably far more common and present in around 15-20% of the population<sup>15</sup>. The prevalence of seborrheic dermatitis is increased among individuals with HIV in whom it may be a presenting sign. The prevalence has been estimated to be around 35 percent among patients with early HIV infection<sup>16</sup>.

### **Irritant or allergic contact dermatitis**

Irritant contact dermatitis (ICD) is an inflammation of the skin typically manifested by erythema, mild edema and scaling. The hands are the most important sites of ICD, which originates from repeated exposure to e.g. soaps, cleansers and solvents. ICD is significantly more common in women than in men, may occur at any age and in extremely highly exposed workers, the prevalence can be as high 69.7%<sup>18</sup>.

Allergic contact dermatitis (ACD) is a delayed type of induced sensitivity (allergy) resulting from skin contact with a specific allergen to which the patient has developed a specific sensitivity, which include nickel, preservatives, dyes and fragrances. The allergic reaction causes an inflammation of the skin manifested by erythema, edema and vesiculation. ACD is more common in women than in men and a Swedish study found that prevalence of hand ACD was 2.7 cases per 1000 population, whereas a Dutch study found that prevalence of hand ACD was 12 cases per 1000 population<sup>19</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 erythematous-to-violaceous, scaly plaques with prominent follicular plugging 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>20</sup>.

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

#### **Dermatoses (eczema, psoriasis, Lichen simplex chronicus)**

Diflucortolone valerate cream (other potent corticosteroid) was compared to betamethasone valerate cream in a study of 138 eczema patients. Results of the comparative study showed both preparations produced excellent results in eczema.

#### **Atopic and nummular dermatitis**

Two or three-week studies compared amcinonide cream (other potent corticosteroid) with betamethasone cream in the treatment of various dermatoses such as atopic dermatitis and seborrheic dermatitis and both drugs were effective and demonstrated similar results.

A study including 72 patients comparing the efficacy of bufexamac cream (other topical anti-inflammatory drug) to betamethasone cream in cases of atopic or contact dermatitis resulted in betamethasone was more effective in relieving pruritus and slightly more efficacious in the treatment of patients under 35 years, while the two treatments were equal for older patients.

Betamethasone valerate cream was compared to fluocinonide cream (other potent corticosteroid) in 40 men and 67 women with atopic dermatitis in a study. Patients were treated twice a day for 3 weeks and displayed clinical responses following both treatments.

#### **Psoriasis**

The efficacy of topical calcipotriene (a synthetic form of vitamin D used in psoriasis) was compared with betamethasone in 409 patients with psoriasis administered twice daily for 6 weeks. Results showed that calcipotriene was as effective as betamethasone valerate. Similar results were also reported in a study including 417 patients using calcipotriol (calcipotriene) in comparison to betamethasone-17-valerate.

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

There are limited data regarding the effect of Bemeson 1mg/g cream on fertility and usage in pregnant women and during breastfeeding.

### **VI.2.4 Summary of safety concerns**

#### **Important identified risks**

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
Hypersensitivity reactions	Betamethasone 17-valerate or any of the excipients in Bemeson cream may cause allergic reactions.	Tell your doctor before starting treatment if you are allergic (hypersensitive) to betamethasone 17-valerate or any of the other ingredients in the product.  Stop using Bemeson cream

Risk	What is known	Preventability
		<p>immediately if you develop an allergic reaction and tell your doctor.</p> <p>Close monitoring.</p>
Opportunistic infections	Bacterial infection is stimulated by the warm, moist conditions within e.g. skin folds or caused by occlusive dressings.	<p>Tell your doctor if you find that the area being treated becomes infected and stop Bemeson cream treatment if the infection spreads and begin treatment for the infection.</p> <p>Only use an occlusive dressing over Bemeson cream if your doctor has told you to. If you are applying Bemeson cream under an occlusive dressing, make sure that the skin is cleansed before a dressing is applied to prevent infections.</p> <p>Do not use Bemeson cream on open wounds.</p> <p>Close monitoring.</p>
Skin disorders including atrophy with long term use	If Bemeson cream is used in large quantities for a prolonged period or if a large area of the body is treated, the product may be absorbed through the skin and into the blood stream which can e.g. result in stretch marks, changes in skin colour and skin atrophy.	<p>Tell your doctor before starting treatment if you suffer from:</p> <ul style="list-style-type: none"> <li>• acne</li> <li>• rosacea</li> <li>• spotty red rash around your mouth (perioral dermatitis)</li> <li>• itchy skin which is not inflamed</li> <li>• itching around the anus or genitals</li> <li>• infected skin (unless the infection is being treated with an anti-infective medicine at the same time)</li> <li>• widespread plaque psoriasis.</li> </ul> <p>Only use Bemeson cream for as long as your doctor recommends. If your condition does not improve with 2 – 4 weeks of treatment, speak to your doctor.</p> <p>If you are applying Bemeson cream in the face, prolonged use</p>

Risk	What is known	Preventability
		<p>is not recommended, as this area is more sensitive to atrophic changes.</p> <p>Close monitoring.</p>
<p>Endocrine disorders/adrenal suppression</p>	<p>When treatment is prolonged, systemic absorption may occur that can cause Cushing's syndrome including weight gain and rounding of the face (moon face) and other symptoms.</p> <p>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 anorexia, nausea, vomiting, abdominal pain, weakness, tiredness, asthenia, prostration, myalgia, arthralgia, weight loss, postural hypotension, somnolence and depression.</p> <p>Continuous treatment or use of occlusion in infants and children can also give rise to adrenocortical suppression and growth retardation.</p>	<p>Do not use large quantities of Bemeson cream for a prolonged period. Only use Bemeson cream for as long as your doctor recommends. If your condition does not improve with 2 - 4 weeks of treatment, speak to your doctor.</p> <p>Do not use Bemeson cream on children below the age of 1 and usage should be avoided for children below the age of 12.</p> <p>Only use an occlusive dressing over Bemeson cream if your doctor has told you to.</p> <p>Close monitoring.</p>
<p>Rebound psoriatic relapses</p>	<p>Topical corticosteroids should be used with caution with psoriasis, as there have been reports of development of relapses</p>	<p>Do only apply Bemeson cream as informed by your doctor.</p> <p>Close monitoring.</p>
<p>Tolerance</p>	<p>Topical corticosteroids should be used with caution with psoriasis, as there have been reports of development of tolerance</p>	<p>Do only apply Bemeson cream as informed by your doctor.</p> <p>Close monitoring.</p>

### Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Overdose/Interaction with other drugs	<p>If Bemeson cream 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. This in turn can result in Cushing's syndrome including weight gain and rounding of the face (moon face).</p> <p>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 stretch marks, changes in skin colour, skin thinning, anorexia, nausea, vomiting, abdominal pain, weakness, tiredness, asthenia, prostration, myalgia, arthralgia, weight loss, postural hypotension, somnolence and depression.</p> <p>If Bemeson cream is used in large quantities and/or for a prolonged period or if a large skin area is treated, the product may be absorbed through the skin and into the blood stream, which in turn might result in the occurrence of interactions with other drugs.</p> <p>Concomitant administration of drugs that may inhibit CYP3A4 example ritonaviror itraconazole should be avoided as it have been shown to inhibit the metabolism of corticosteroids, leading to increased systemic exposure.</p>
Eye disorders	Application of Bemeson cream onto the eyelids may result in that the product comes into the eyes and thereby, there is a risk of developing glaucoma or cataract
Use during pregnancy	There are limited data regarding effect of Bemeson cream in the pregnancy.

### Missing information

Risk	What is known
Use in breastfeeding and effect on fertility	There are limited data regarding effect of Bemeson cream on fertility and breastfeeding.
Use in children under the age of 12	<p>Betamethasone valerate should not be used in children, as safety and efficacy in the pediatric population cannot be clarified.</p> <p>Betamethasone valerate is contraindicated in skin diseases in children under 1 year, including dermatitis.</p> <p>Children may be more susceptible than adults to topical corticosteroid-induced HPA axis suppression and to exogenous corticosteroid effects, due to the large skin surface as compared to the body weight.</p>

**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.

**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.