COMMITTEE OF EXPERTS
ON THE CLASSIFICATION OF MEDICINES
AS REGARDS THEIR SUPPLY
(CD-P-PH/PHO)

Evidence-based classification reviews of medicines
belonging to the ATC group D07A
(Corticosteroids, Plain)

2019

Table of Contents

INTRODUCTION

The availability of medicines with or without a medical prescription has implications on patient safety, accessibility of medicines to patients and responsible management of healthcare expenditure.

The decision on prescription status and related supply conditions is a core competency of national health authorities. The conditions of the supply of medicines vary considerably in Council of Europe member states, due to the fact that the provisions are differently interpreted and implemented by the member states, and that important additional classification criteria are not harmonised.

The Committee of Experts on the Classification of Medicines as regards their Supply (CD-P-PH/PHO)[1] is co-ordinated by the European Directorate for the Quality of Medicines and HealthCare (EDQM, Council of Europe) and its working programme is based on Committee of Ministers Resolution CM/Res(2018)1 on the classification of medicines as regards their supply[2].

In its work, the CD-P-PH/PHO focuses on public health promotion and uses scientific approaches, taking account of the national assessments of direct and indirect risks which may occur under normal treatment conditions and under medical surveillance, as well as from foreseeable misuse or abuse of medicines.

The CD-P-PH/PHO issues twice a year recommendations to health authorities of Council of Europe member states (EU and non-EU member states) on the classification of medicines and establishes good classification practices.

The recommendations are also useful for pharmaceutical manufacturers and commercial operators of mail-order trade in medicines where such trade is legal.

A pioneer in this field, Council of Europe bodies have been concerned since 1961 with issues relating to the classification of medicines into prescription and non-prescription medicines and have inspired relevant EU legislation.

The classification criteria set out in the Council of Europe resolutions have been supplanted by Directives 92/26/CEE and 2001/83/EC (art. 70-75). Directive 2001/83/EC refers to the Council of Europe in its Whereas 32: "*It is therefore appropriate, as an initial step, to harmonise the basic principles applicable to the classification for the supply of medicinal products in the Community or in the Member State concerned, while taking as a starting point the principles already established on this subject by the Council of Europe"*[3].

It is important to note that:

- The CD-P-PH/PHO does not issue recommendations on the classification of particular medicines, but on active substances used in a medicine for a specific therapeutic purpose.

- In its work, the CD-P-PH/PHO uses the Anatomical Therapeutic Chemical (ATC) classification maintained by the WHO Collaborating Centre for Drug Statistics Methodology[4] to identify active substances or combinations of active substances.

- The CD-P-PH/PHO does not give advice relating to pending marketing authorisation procedures.

The CD-P-PH/PHO supervises a database (i.e. *Melclass*[5]), hosted by the EDQM, which stores the recommendations that the Committee of Experts issues twice a year to health authorities of the

[1] http://go.edqm.eu/PHO

[2] http://go.edqm.eu/CMRes20181

[3] https://goo.gl/at4RZo

[4] https://goo.gl/KvqKir

[5] https://melclass.edqm.eu/

Council of Europe member states which are parties to the Convention on the Elaboration of a European Pharmacopoeia, as well as national information about the classification status and supply conditions of medicines in these member states. The information is publicly available. Recommendations about 2100 medicines are published in the *Melclass* database.

Providing a platform for dialogue and consensus building on the supply conditions of medicines in Europe as facilitated by Council of Europe Committee of Ministers Resolution CM/Res(2018)1, the CD-P-PH/PHO promotes patient safety and, where appropriate, access to medicines without a prescription across Europe, which helps to foster public health and to responsibly manage healthcare resources.

DISCLAIMER

This document is published for information only.

The reports included in this document have no legal status and no binding character.

They reflect the debates and conclusions of the reviews of scientific classifications of medicines that took place at the 2019 bi-annual meetings of the CD-P-PH/PHO. The document was reviewed and endorsed by the CD-P-PH/PHO at its 67th meeting (December 2019).

The reviews carried out do not commit the parent authorities of the experts nor the Council of Europe/EDQM.

GLOSSARY OF TERMS USED IN THIS DOCUMENT

ACTH	Adrenocorticotropic hormone
ATC	Anatomical Therapeutic Chemical classification [1]
CSC	Central serous chorioretinopathy
EDQM	European Directorate for the Quality of Medicines and HealthCare
EMA	European Medicines Agency
GSL	General sales list medication
HPA	Hypothalamic-pituitary-adrenal
MDD	Maximal daily dose
MQP	Maximal quantity per pack
MS	Maximal strength
P	Pharmacy-only medication
POM	Prescription only medicine
SmPC	Summary of product characteristics
WHO	World Health Organization

Classification used throughout this document

Following the stipulations of Resolution CM/Res(2018)1, the lists of active substances classified according to the conditions of supply of the medicines which contain them are drawn up with reference to all the risks, direct or indirect, which they may represent to human health whether they are used in accordance with the product information leaflet or not.

The differentiation into two prescription lists (List I and List II) applies only to the countries which classify prescription medicines into two categories based on whether the prescription can be renewed or not.

1. Active substances in medicines subject to prescription

List I: the supply of a medicine containing one of the substances in this list should not be renewed without the prescriber having so specified. This classification should apply to active substances of medicines indicated for conditions calling for short-term treatment and/or for which continuous medical supervision is necessary, either because of potential undesirable effects or to check the efficacy of treatment; or active substances of medicines administered for diagnostic purposes; or active substances with a new pharmacological mechanism of action.

List II: the supply of a medicine containing one of the substances in this list can be renewed. This classification should apply to active substances in medicines indicated for conditions for which the patient may continue the regular or intermittent treatment without new medical advice, and for which well-known undesirable effects do not call for frequent clinical examination.

Exemptions from Lists I and II under certain circumstances: depending on the conditions of use of the medicine, active substances contained in prescription medicines may also be contained in medicines classified under the same ATC code but which are not subject to prescription.

Under certain circumstances, exemptions from the prescription requirement may be set out in the Melclass database:

- in respect of a low dosage or concentration of the active substances and/or the therapeutic indications of medicines in which they are contained;
- according to the route of administration and the composition of the medicine;
- according to the total amount of the medicine per container.

2. List of active substances in medicines not subject to prescription: active substances in medicines which are not classified as subject to prescription in Lists I or II.

[1] World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology - https://goo.gl/KvqKir

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Methylprednisolone

1.2 ATC code: D07AA01

1.3 Therapeutic indications: treatment of various skin disorders, such as atopic dermatitis, allergic eczema.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are only authorised in Georgia (classification status: POM)).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, medicines containing this active substance are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference – 38th Edition

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Hydrocortisone

1.2 ATC code: D07AA02

1.3 Therapeutic indications: for the treatment of contact and allergic dermatitis, insect bite reactions and mild to moderate eczema, prurigo nodularis, neurodermatosis, seborrhoeic dermatitis, intertrigo and contact sensitivity reactions.

1.4 Posology and duration of treatment: adults and children over 12 years: For use on the skin only. It should be applied sparingly once or twice a day to the affected area, or as directed by the physician. It should not be used for more than 7 days.

1.5 Pharmaceutical forms: cream, lotion or ointment. Usually in concentrations of 0.1-2.5%.

1.6 Contraindications: use in the presence of untreated infections of bacterial, viral, tuberculous or fungal origin. Use in acne vulgaris, acne rosacea or in perioral dermatoses.

1.7 Relevant warnings: the product should not be used on the anal or genital region, or on broken or infected skin. The product should not be used on the face except on medical advice. Continuous treatment for longer than 3 weeks should be avoided in patients under the age of 3 years because of the possibility of adrenocortical suppression or of growth suppression. Prolonged use of uninterrupted occlusion or use with extensive occlusive dressings, including napkins, may suppress adrenocortical function. Continuous application without interruption will result in local atrophy of the skin, striae and superficial vascular dilatation, particularly on the face. There have been a few reports in the literature of the development of cataracts in patients who have been using corticosteroids for prolonged periods of time.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): rarely, local sensitivity may occur, requiring discontinuation of treatment.

2.2 Indirect risks (incorrect use): topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered necessary.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
Austria (AT)	List I					
Belgium (BE)	Not subject to prescription		1%			
Bosnia and Herzegovina (BiH)	POM				300 mg	Cutaneous use
Switzerland (CH)	List II + Exemption		Ex.: 5.0 mg		Ex.: 15 g	Cutaneous use
Czech Republic (CZ)	Not subject to prescription	Local inflammatory or allergic cutaneous diseases.	1%		100 mg	Cutaneous use. Maximum duration of therapy without medical advice: 14 days.
Estonia (EE)	POM + Exemption		1%		10 g	Cutaneous use
Spain (ES)	POM + Exemption		Ex.: 0.5%		Ex.: 50 g	
Finland (FI)	POM + Exemption		Ex.: 1%		Ex.: 50 g	Rectal use

France (FR)	List I + Exemption		Ex.: 0.5%		Ex.: 15 g	Cutaneous use
Croatia (HR)	Not authorised					
Hungary (HU)	POM					
Ireland (IE)	List II + Exemption		Ex.: 1%		Ex.: 15 g	Cutaneous use
Italy (IT)	List II + Exemption		Ex.: 0.5%		Ex.: 20 g	Cutaneous use
Lithuania (LT)	POM + Exemption		Ex.: 1%		Ex.: 10 g	Cutaneous use
Latvia (LV)	POM					
North Macedonia (MK)	POM					
Netherlands (NL)	POM					
Poland (PL)	POM + Exemption		Ex.: 1%		Ex.: 15 g	Cutaneous use
Portugal (PT)	Not subject to prescription					
Romania (RO)	List I					
Serbia (RS)	POM					
Sweden (SE)	POM + Exemption		Ex.: 1%		Ex.: 50 g	Cutaneous use
Slovenia (SI)	Not subject to prescription					

No more data available from other member states.

Melclass database[1]: I + Exemption

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I + Exemption**

Exemptions: cutaneous use; for adults and children over 12 years of age; indication: treatment of contact and allergic dermatitis, insect bite reactions and mild to moderate eczema; MS: 1%; MQP: 15 g.

Criteria: short-term treatment only; exemptions: conditions or symptoms (eczema, dermatitis, allergic dermatitis) for which the product is indicated can be correctly diagnosed without medical supervision. Administration is limited to adults and children over 12 and duration of treatment is limited to 7 days.

3.2.2 Paediatric use: not to be used on children under 12 years of age unless under medical supervision. If symptoms persist a physician should be consulted.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference (last update: 12.03.2019)

Medicines and Medical Devices Agency of Serbia (ALIMS): https://bit.ly/2Wag33e

Health Products Regulatory Authority (HPRA) (Ireland): https://bit.ly/2HofV8q

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Prednisolone

1.2 ATC code: D07AA03

1.3 Therapeutic indications: skin disorders that respond to local glucocorticoid therapy, such as: acute, subacute and chronic eczema; dermatitis; pruritus; erythema exudative multiforme; scalds and burns of the first degree; sunburns.

1.4 Posology and duration of treatment: the product should be applied topically in a thin layer, 2-3 times a day, on the affected skin area. Duration of treatment should not exceed 2 weeks.

1.5 Pharmaceutical forms: cream and ointment 0.15%.

1.6 Contraindications: skin diseases accompanied by bacterial, viral or fungal infections. Rosacea, perioral dermatitis.

1.7 Relevant warnings: for prolonged or extensive application, especially under occlusion and on mucous membranes, the possibility of systemic absorption cannot be excluded. The risk of secondary skin infections is increased with the use of glucocorticoids. Visual disturbance may be reported with systemic and topical corticosteroid use.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): skin atrophy, pigmentation changes, exacerbation of underlying symptoms, local skin burning, hypertrichosis, rash, pruritus, erythema. Blurred vision.

2.2 Indirect risks (incorrect use): even at very high doses, no signs of systemic glucocorticoid overdose are expected.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AT	List I					
BE	Not authorised					
BiH	Not authorised					
CH	List II					
CZ	Not authorised					
EE	Not authorised					
ES	Not authorised					
FI	Not authorised					
FR	Not authorised					
HR	List I					
HU	POM					
IE	List II					
IT	Not authorised					
LT	Not authorised					
LV	Not authorised					
MK	Not authorised					
NO	Not authorised					

NL	Not authorised					
PL	Not authorised					
PT	Not authorised					
RO	Not authorised					
RS	Not authorised					
SE	Not authorised					
SI	Not authorised					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term treatment and medical supervision required.

3.2.2 Paediatric use: in infants and toddlers under 1 year, no glucocorticoids should be used.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference (last update: 12.03.2019)

Austrian Medicines and Medical Devices Agency (AGES): https://bit.ly/2w4hjWY

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Clobetasone

1.2 ATC code: D07AB01

1.3 Therapeutic indications: clobetasone is indicated for adults, the elderly, children and infants for the relief of the inflammatory and pruritic manifestations of steroid-responsive dermatoses. These include: atopic dermatitis; irritant or allergic contact dermatitis; seborrheic dermatitis; nappy rash; photodermatitis; otitis externa; prurigo nodularis; insect bite reactions.

1.4 Posology and duration of treatment: preparations should be thinly and gently rubbed in using only enough to cover the entire affected area once or twice a day until improvement occurs, then the frequency of application should be reduced or treatment should be changed to a less potent preparation. Adequate time for absorption should be allowed after each application before applying an emollient. Continuous daily treatment for longer than 4 weeks is not recommended. If the condition worsens or does not improve within 4 weeks, treatment and diagnosis should be re-evaluated.

1.5 Pharmaceutical forms: cream 0.05%; ointment 0.05%

1.6 Contraindications: untreated cutaneous infection; rosacea; acne vulgaris; pruritus without inflammation.

1.7 Relevant warnings: clobetasone should be used with caution in patients with a history of local hypersensitivity to other corticosteroids. Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, leading to glucocorticosteroid insufficiency can occur in some individuals as a result of increased systemic absorption of topical steroids. During the use of topical corticosteroids, there is potential risk for increased systemic effects (risk factors: potency and formulation of topical steroid, duration of exposure, application to a large surface area, use on occluded areas of skin, use on thin or broken skin). Children are more likely to develop local and systemic adverse reactions due to the use of local corticosteroids because of their higher surface area to body mass ratio and, in general, require a shorter treatment. Particularly, in infants and toddlers the nappy can be considered as an occlusive dressing and therefore can enhance absorption. In infants and children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal and growth suppression is more likely to occur. Visual disturbance may be reported with systemic and topical corticosteroid use.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): the following adverse reactions have been reported: opportunistic infection (very rare); hypersensitivity and generalised rash (very rare); HPA-axis suppression, Cushingoid features (e.g. moon face, central obesity), delayed weight gain/growth retardation in children, osteoporosis, glaucoma, hyperglycaemia/glucosuria, cataract, hypertension, increased weight/obesity, decreased endogenous cortisol level (very rare); allergic contact dermatitis, urticaria, skin atrophy, pigmentation changes, exacerbation of underlying symptoms, local skin burning, hypertrichosis, rash, pruritus, erythema (very rare); blurred vision (not known).

2.2 Indirect risks (incorrect use): topically applied clobetasone may be absorbed in sufficient amounts to produce systemic effects. Acute overdosage is very unlikely to occur; however, in the case of chronic overdosage or misuse, the features of hypercortisolism may occur.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AT	List I					
BE	POM					
BiH	Not authorised					
CH	List II					
CZ	Not authorised					
EE	Not authorised					
ES	POM					
FI	POM					
FR	Not authorised					
DE	POM					
GE	Not authorised					
HR	Not authorised					
HU	Not authorised					
IE	List II					
IT	List II					
LT	Not authorised					
LV	Not authorised					
MK	Not authorised					
NL	POM					
PL	Not authorised					
PT	POM					
RO	Not authorised					
RS	Not authorised					
SE	POM					
SI	Not authorised					
United Kingdom (UK)	POM+ Exemption	Short-term symptomatic treatment and control of patches of eczema and dermatitis (excluding seborrheic dermatitis) in adults and in children aged 12 years and over	Ex. 0.05%		Ex. 15.0 g	Cutaneous use

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term treatment under medical supervision.

3.2.2 Paediatric use: use in children under 12 years should be on the advice of a doctor. Care should be taken when using clobetasone to ensure the amount applied is the minimum that provides therapeutic benefit. Treatment should not normally exceed 7 days.

3.2.3 Social dimension: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference (last update: 12.03.2019)

Medicines and Healthcare products Regulatory Agency (MHRA) (United Kingdom): https://bit.ly/2VDANBc

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Hydrocortisone butyrate

1.2 ATC code: D07AB02

1.3 Therapeutic indications: for the treatment of conditions responsive to topical corticosteroids, e.g. eczema, dermatitis and psoriasis not caused by micro-organisms. Topical corticosteroids are not generally indicated in psoriasis but may be acceptable in psoriasis excluding widespread plaque psoriasis.

1.4 Posology and duration of treatment: for topical application. Dosage: to be applied evenly and sparingly one to three times daily.

1.5 Pharmaceutical forms: cream 0.1% w/w; ointment 0.1% w/w; emulsion for skin 0.1% w/w; solution for skin 0.1% w/w.

1.6 Contraindications: presence of untreated viral or fungal infections (mycotic yeast) or parasitic infections, tubercular or syphilitic lesions, ulcerous skin lesions, perioral dermatitis, acne vulgaris and rosacea and in bacterial infections unless used in connection with appropriate chemotherapy.

1.7 Relevant warnings: extreme caution is required in dermatoses of infancy including napkin eruption. In such patients courses of treatment should not normally exceed 7 days. Application under occlusion should be restricted to dermatoses involving limited areas. Application to the face, flexures and other areas of thin skin (pilous and genital skin) may cause skin atrophy and increased absorption and should be avoided. Absorption of corticosteroids can be greatly increased when applied to large areas, in particular to skin folds and under (plastic) occlusion, leading to suppression of adrenal cortex function. This can occur quite quickly in children and can lead to suppression of growth hormone secretion. Visual disturbance may be reported with systemic and topical corticosteroid use.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): adrenal suppression (very rare); hypersensitivity (not known); skin atrophy, often irreversible, with thinning of the epidermis; telangiectasia; purpura; skin striae; pustular acne; perioral dermatitis; rebound effect; skin depigmentation; dermatitis and eczema including contact dermatitis (rare).

2.2 Indirect risks (incorrect use): excessive use, especially under occlusive dressings or over a long period of time, may produce adrenal suppression. No special procedures or antidote.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AT	Not authorised					
BE	POM					
BiH	Not authorised					
CH	List II					
DE	POM					
EE	Not authorised					
ES	POM					
FI	POM					
FR	List I					

GE	Not subject to prescription					
HR	Not authorised					
IE	List II					
IT	List II					
LT	POM					
LV	POM					
MK	Not authorised					
NL	POM					
PL	POM					
PT	POM					
RO	List I					
RS	Not authorised					
SE	POM					
SI	POM					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term treatment and medical supervision required.

3.2.2 Paediatric use: long-term treatment should be avoided and occlusion should not be used. Courses should be limited to 7 days where possible.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference (last update: 12.03.2019)

HPRA: https://bit.ly/2VoZQD7

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Flumetasone

1.2 ATC code: D07AB03

1.3 Therapeutic indications: flumetasone is a corticosteroid used topically for its glucocorticoid activity in the treatment of various skin disorders.

1.4 Posology and duration of treatment: depending on the severity of the condition, flumetasone should be spread in a thin layer once or twice a day over the area to be treated. If necessary, the cream or ointment should be rubbed in with light friction.

1.5 Pharmaceutical forms: it is usually used as a 0.02% cream, ointment or lotion.

1.6 Contraindications: hypersensitivity to the active ingredient, to corticosteroids in general or to one of the excipients according to the product composition. Contraindicated in cases of bacterial and viral skin diseases (e.g. pyoderma, chickenpox, vaccinia, herpes simplex, shingles), fungal skin diseases, syphilis, skin tuberculosis, skin ulcers, vaccine rash, rosacea, perioral dermatitis, acne vulgaris, application to the eye.

1.7 Relevant warnings: exceptional use of flumetasone in high doses, on large areas of skin or under occlusive dressings should be done under regular medical supervision of the patient, particularly with regard to suppression of endogenous corticosteroid synthesis. The risk of an influence on the HPA-axis exists mainly in small children during long-term use. No specific studies have been conducted in children and adolescents (2-17 years). The use of flumetasone is therefore not recommended in children and adolescents. If treatment with a dermatological product containing flumetasone is medically necessary in children, the medication should only be applied to small areas (less than 10% of the body surface area) and for a short period of time (maximum 2 weeks, without using an occlusive dressing and without applying it to intertriginous areas). In infants, flumetasone should be used only when absolutely necessary, for no longer than 7 days and at the lowest clinically effective dose. Whenever possible, continuous application should not exceed 2-3 weeks. Corticosteroids of high or medium potency should be used on the face or genital area only with caution and for no longer than 1 week. This applies to all age groups. As a matter of principle, only low-potency corticosteroids should be applied near the eyes (glaucoma). In the case of infections and skin ulcers, local corticosteroids should only be used with special care and with additional treatment of the infection. Based on experience to date, percutaneous absorption of flumetasone is not detectable, so that systemic adverse effects such as a clinically important influence on adrenal cortical function are hardly to be expected, provided the product is used as recommended. As a matter of medical principle, this risk should nevertheless be considered, especially in paediatric use, as prolonged use of local corticosteroids may lead to adrenal suppression and Cushing's syndrome. Application under an occlusive dressing should be time-limited and reserved for small dermatoses. Treatment of psoriasis with topical corticosteroids may be associated with relapses on abrupt discontinuation of treatment (rebound effect), development of tolerance and the onset of generalised pustular psoriasis. If this drug is used to treat psoriasis, it is therefore important to monitor the patient closely. Corticosteroids may mask the symptoms of an allergic skin reaction to one of the components of the preparation. The patient should be instructed to use the preparation only for the treatment of his or her current skin condition and not to pass the drug on to others. Visual disturbances may occur with systemic and topical use of corticosteroids. If a patient presents with symptoms such as blurred vision or other visual disturbances, which include, but are not limited to, cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSC), which have been reported following the use of systemic or topical corticosteroids, an ophthalmologic consultation should be scheduled to assess the possible causes of this disorder.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): Infections and infestations: unknown frequency: secondary infections due to a decrease in local immune defences.

Endocrine disorders: frequency unknown: suppression of endogenous corticosteroid synthesis, hypercorticosteroidism with oedema, diabetes mellitus, osteoporosis and growth retardation in children.

Eye conditions: uncommon: blurred vision.

Skin and subcutaneous tissue disorders: rare: slight skin atrophy, stretch marks, telangiectasia, purpura, acne, allergic dermatitis, rosacea, dermatitis, dry skin. Unknown frequency: hyperpigmentation of the skin.

General disorders and anomalies at the administration site: rare: slight irritation at the application site, as well as signs of burning, rash, pruritus limited to the application site. Frequency unknown: wound healing disorders.

2.2 Indirect risks (incorrect use): although there are no reports to date of overdosage with flumetasone, prolonged application of local corticosteroids may result in adrenal suppression or Cushing's syndrome, and adverse reactions may be more frequent.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AT	Not authorised					
BE	POM					
BiH	Not authorised					
CH	List II					
DE	POM					
ES	Not authorised					
FI	Not authorised					
FR	Not authorised					
GE	Not authorised					
HR	Not authorised					
HU	Not authorised					
IE	Not authorised					
IT	Not authorised					
LT	Not authorised					
LV	Not authorised					
MK	Not authorised					
NL	POM					
PL	Not authorised					
PT	Not authorised					
RO	Not authorised					
RS	Not authorised					
SE	Not authorised					
SI	Not authorised					

No more data available from other member states.

Melclass database[1]: Currently not available

3.2 Social dimension of classification:

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term treatment and medical supervision required.

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference (last update: 12.03.2019)

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluocortin

1.2 ATC code: D07AB04

1.3 Therapeutic indications: Acute mild or moderate exogenous eczema and endogenous eczema (atopic dermatitis, neurodermatitis), seborrheic eczema.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference – 38th Edition

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluperolone

1.2 ATC code: D07AB05

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference – 38th Edition

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluorometholone

1.2 ATC code: D07AB06

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference – 38th Edition

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluprednidene

1.2 ATC code: D07AB07

1.3 Therapeutic indications: for the treatment of inflammatory skin diseases where topical application of moderately potent glucocorticoids is indicated, e.g. atopic eczema (atopic dermatitis, endogenous eczema), contact dermatitis.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are only authorised in Austria (legal status: List I) and Germany (legal status: POM)).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, medicines containing this active substance are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference – 38th Edition

AGES: https://bit.ly/2Q8cQvH

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Desonide

1.2 ATC code: D07AB08

1.3 Therapeutic indications: desonide is a corticosteroid used topically for its glucocorticoid activity in the treatment of various skin disorders (e.g. contact eczema, atopic dermatitis, seborrheic dermatitis, insect bites).

1.4 Posology and duration of treatment: treatment should be limited to 2 applications per day. An excessive increase in the number of daily applications may aggravate the adverse effects without improving the therapeutic effects.

1.5 Pharmaceutical forms: it is usually used as a cream, ointment, lotion, gel or foam containing 0.05% or 0.1%.

1.6 Contraindications: bacterial, viral or fungal skin infection; ulcerated lesions; acne; rosacea; perioral dermatitis.

1.7 Relevant warnings: application to the face may cause skin atrophy and increased absorption and should be avoided. Visual disturbance may be reported with systemic and topical corticosteroid use. During the use of topical corticosteroids, there is potential risk for increased systemic effects (risk factors: potency and formulation of topical steroid, duration of exposure, application to a large surface area, use on occluded areas of skin, use on thin or broken skin).

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): as with other topical corticosteroids, prolonged use of large amounts or treatment of a large area may result in adrenal suppression. This effect is more likely to occur in infants and children and when using occlusive dressings. With use of topical corticosteroids there is a potential for systemic effects including suppression of the HPA-axis, Cushing's syndrome, delayed growth and development in children, blurred vision. Secondary infections, especially under occlusive dressing, and allergic contact dermatoses have also been reported with the use of local corticosteroids.

2.2 Indirect risks (incorrect use): the risk of acute overdose is unlikely. However, in case of excessive or prolonged use of local corticosteroids, the risk of exacerbation of adverse effects and the possibility of systemic effects should not be ruled out.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AT	Not authorised					
BE	Not authorised					
BiH	Not authorised					
CH	List II					
CZ	Not authorised					
DE	Not authorised					
EE	Not authorised					
ES	Not authorised					
FI	POM					
FR	List I					

GE	Not subject to prescription					
HR	Not authorised					
IE	Not authorised					
IT	List II					
LT	Not authorised					
LV	Not authorised					
MK	Not authorised					
NL	Not authorised					
PL	Not authorised					
PT	POM					
RO	Not authorised					
RS	Not authorised					
SE	Not authorised					
SI	Not authorised					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term treatment under medical supervision.

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference (last update: 12.03.2019)

National Agency for the Safety of Medicine and Health Products (ANSM) (France): https://bit.ly/2HtMgt9

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Triamcinolone

1.2 ATC code: D07AB09

1.3 Therapeutic indications: dermatoses, allergic or nonspecific inflammations which respond to a local corticoid treatment and in which the use of a moderately potent corticoid is indicated, such as acute and chronic forms of eczema. Psoriasis vulgaris with high inflammatory activity.

1.4 Posology and duration of treatment: duration of therapy should not exceed 4 weeks. Triamcinolone is applied once or twice daily to the affected skin areas.

1.5 Pharmaceutical forms: for topical application in the treatment of various skin disorders triamcinolone is usually used as creams, lotions or ointments containing 0.1%, although concentrations ranging from 0.025 to 0.5% have been employed.

1.6 Contraindications: varicella and other viral infections, vaccination reactions, bacterial infections or mycoses, especially in the application area. During pregnancy. Not to be used in rosacea and perioral dermatitis.

1.7 Relevant warnings: not suitable for use on the eyes. In infants and toddlers long-term treatment should be avoided. It should therefore be used in children for as short a period as possible (less than 7 days) with the lowest possible dose ensuring therapeutic efficacy. Visual disturbance may be reported with systemic and topical corticosteroid use.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): in occasional cases, hypersensitivity reactions may occur, e.g. in the form of burning, itching, irritation, dry skin, allergic contact dermatitis. Prolonged use on large areas may occasionally lead to skin atrophy, and in extreme cases to ulcer, telangiectasia, striae, steroid acne, folliculitis, hypertrichosis, pigmentary displacement, perioral dermatitis and secondary infections. Manifestations of hypercortisolism (Cushing's syndrome) and reversible HPA-axis suppression leading to glucocorticosteroid insufficiency can occur in some individuals as a result of increased systemic absorption of topical steroids. Blurred vision (not known).

2.2 Indirect risks (incorrect use): prolonged and excessive use may lead to local irritation, skin atrophy and suppression of adrenocortical function due to increased absorption.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AT	List I					
BE	Not subject to prescription					
BiH	Not authorised					
CH	Not authorised					
CZ	POM					
DE	Not authorised					
EE	POM					
ES	Not authorised					
FI	Not authorised					
FR	Not authorised					

GE	Not subject to prescription					
HR	Not authorised					
HU	POM					
IE	Not authorised					
IT	List II					
LT	POM					
LV	POM					
MK	Not authorised					
NL	POM					
PL	Not authorised					
PT	Not authorised					
RO	List I					
RS	Not authorised					
SE	Not authorised					
SI	Not authorised					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term treatment and medical supervision required.

3.2.2 Paediatric use: in infants and toddlers long-term treatment should be avoided. It should therefore be used in children for as short a period as possible (less than 7 days) with the lowest possible dose ensuring therapeutic efficacy.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference (last update: 12.03.2019)

AGES: https://bit.ly/2JIlLCV

Republic State Institute for Drug Control (SUKL) (Czech Republic): https://bit.ly/2WLuyb9

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Alclometasone

1.2 ATC code: D07AB10

1.3 Therapeutic indications: for the treatment of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

1.4 Posology and duration of treatment: for adults and children, a thin film should be applied to the affected area two or three times daily or as directed by the physician. If there is no improvement in 2 weeks, the diagnosis should be re-evaluated.

1.5 Pharmaceutical forms: it is usually used as a cream or ointment containing 0.05%.

1.6 Contraindications: use in the presence of untreated infections of bacterial, viral tuberculous or fungal origin. Use in acne rosacea, acne vulgaris or in perioral dermatoses.

1.7 Relevant warnings: long-term continuous therapy should be avoided in all patients irrespective of age due to increased risk of adrenocortical suppression. Continuous treatment for longer than 2 weeks should be avoided in children. Systemic absorption of topical corticosteroids may be increased if extensive body surface areas are treated or if the occlusive technique is used. Suitable precautions should be taken under these conditions or when long-term use is anticipated, particularly in infants and children.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): adverse reactions reported rarely with alclometasone dipropionate are itching, burning, erythema, dryness, irritation and papular rashes. Other local adverse reactions associated with topical corticosteroids, especially under occlusive dressings, include folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, skin maceration, secondary infection, skin atrophy, striae and miliaria. Continuous application without interruption will result in local atrophy of the skin, striae and superficial vascular dilation, particularly on the face.

2.2 Indirect risks (incorrect use): acute overdosage with dermatologic application of corticosteroids is unlikely and would not be expected to lead to a life-threatening situation. Excessive or prolonged use of topical corticosteroids can suppress pituitary-adrenal function, resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AT	Not authorised					
BE	Not authorised					
BiH	POM					
CH	Not authorised					
CZ	POM					
DE	Not authorised					
EE	Not authorised					
ES	Not authorised					
FI	Not authorised					
FR	Not authorised					

HR	List I					
HU	Not authorised					
IE	List II					
IT	Not authorised					
LT	Not authorised					
LV	Not authorised					
MK	POM					
NL	Not authorised					
PL	POM					
PT	Not authorised					
RO	Not authorised					
RS	POM					
SE	Not authorised					
SI	POM					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term treatment and medical supervision required.

3.2.2 Paediatric use: paediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA-axis suppression and to exogenous corticosteroid effects than mature patients because of greater absorption due to a larger skin surface area to body weight ratio. 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 adrenocorticotropic hormone (ACTH) stimulation. Manifestations of intracranial hypertension include a bulging fontanelle, headaches and bilateral papilledema.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference (last update: 12.03.2019)

ALIMS: https://www.alims.gov.rs/ciril/files/lekovi/smpc/515-01-02690-16-001.pdf

HPRA: https://bit.ly/2HzBt0K

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Hydrocortisone buteprate

1.2 ATC code: D07AB11

1.3 Therapeutic indications: for topical application in the treatment of various skin disorders.

1 1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are only authorised in Germany (legal status: POM) and Portugal (legal status: POM)).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, medicines containing this active substance are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference – 38th Edition

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Dexamethasone

1.2 ATC code: D07AB19

1.3 Therapeutic indications: for topical application in the treatment of various skin disorders, such as allergic skin diseases, acute contact eczema, reactions after insect bites.

1.4 Posology and duration of treatment: the product should be applied to the affected area two or four times daily.

1.5 Pharmaceutical forms: creams, ointments, lotions, skin spray. Concentrations usually used have ranged from 0.02 to 0.1%.

1.6 Contraindications: use in the presence of untreated infections of bacterial, viral tuberculous or fungal origin. Use in acne rosacea, acne vulgaris or in perioral dermatoses.

1.7 Relevant warnings: contact of the medicinal product with mucous membranes should be avoided. Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, leading to glucocorticosteroid insufficiency can occur in some individuals as a result of increased systemic absorption of topical steroids. During the use of topical corticosteroids, there is potential risk for increased systemic effects (risk factors: potency and formulation of topical steroid, duration of exposure, application to a large surface area, use on occluded areas of skin, use on thin or broken skin).

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): dexamethasone may cause local side effects such as burning, pruritus, irritation at the site of application, excessive drying, skin lesions, contact dermatitis, perioral dermatitis, maceration of the skin, acne-like changes, stretch marks, rash, hirsutism, skin discoloration, secondary cutaneous infection and folliculitis.

2.2 Indirect risks (incorrect use): during long-term use of the product and/or on large areas of the skin, dexamethasone may be absorbed into the circulation and this can lead to systemic side effects typical for corticosteroids.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AT	Not authorised					
BE	Not authorised					
BiH	Not authorised					
CH	Not authorised					
CZ	Not authorised					
DE	POM					
EE	Not authorised					
ES	Not authorised					
FI	Not authorised					
FR	Not authorised					
GE	Not subject to prescription					
HR	Not authorised					

HU	Not authorised					
IE	Not authorised					
IT	List II					
LT	Not authorised					
LV	Not authorised					
MK	Not authorised					
NL	Not authorised					
PL	POM					
PT	POM					
RO	Not authorised					
RS	Not authorised					
SE	Not authorised					
SI	Not authorised					

No more data available from other member states.

Melclass database[1]: Currently not available

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term treatment and medical supervision required.

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference (last update: 12.03.2019)

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. Therapeutic profile

1.1 Active ingredient: Clocortolone

1.2 ATC code: D07AB21

1.3 Therapeutic indications: clocortolone is a mid-potency topical corticosteroid available as a 0.1% emollient cream approved by the United States Food and Drug Administration for use in the treatment of corticosteroid-responsive dermatoses (inflamed and fissured skin, such as eczematous dermatoses).

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference – 38th Edition

J.Q. del Rosso and L. Kircik. A Comprehensive Review of Clocortolone Pivalate 0.1% Cream - Structural Development, Formulation Characteristics, and Studies Supporting Treatment of Corticosteroid-responsive Dermatoses. J Clin Aesthet Dermatol 2012; 5(7): 20-24. Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3396454/

U.S. Food and Drug Administration(FDA): https://www.fda.gov/Drugs/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Combinations of Corticosteroids

1.2 ATC code: D07AB30

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing combinations of corticosteroids are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing combinations of corticosteroids are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Betamethasone

1.2 ATC code: D07AC01

1.3 Therapeutic indications: betamethasone is indicated for the treatment of eczema and dermatitis of all types, including atopic eczema, photodermatitis, lichen planus, lichen simplex, prurigo nodularis, discoid lupus erythematosus, necrobiosis lipoidica, pretibial myxoedema and erythroderma. It is also effective in the less responsive conditions such as psoriasis of the scalp and chronic plaque psoriasis of the hands and feet, but excluding widespread plaque psoriasis.

1.4 Posology and duration of treatment: adults and children: once to twice daily. In most cases, a thin film of betamethasone cream should be applied to cover the affected area twice daily. For some patients adequate maintenance therapy may be achieved with less frequent application. Cream is especially appropriate for moist or weeping surfaces and the ointment for dry, lichenified or scaly lesions but this is not invariably so. Control over the dosage regimen may be achieved during intermittent and maintenance therapy by using base cream or ointment, the base vehicles of betamethasone cream and ointment. Such control may be necessary in mild and improving dry skin conditions requiring low dose steroid treatment.

NOTE: children: according to the summary of product characteristics (SmPC) for betamethasone valerate for topical use, it may be used in children above 1 year of age, while no data was found about age limit in the SmPC for betamethasone dipropionate.

1.5 Pharmaceutical forms: cream and ointment 0.025%, 0.05%, 0.1%; lotion 0.1%; cutaneous foam 0.1%.

1.6 Contraindications: rosacea, acne, perioral dermatitis, perianal and genital pruritus. Hypersensitivity to any of the ingredients of the betamethasone presentations contraindicates their use as do tuberculous and most viral lesions of the skin, particularly herpes simplex, vaccinia, varicella. Betamethasone should not be used in napkin eruptions, fungal or bacterial skin infections without suitable concomitant anti-infective therapy.

1.7 Relevant warnings: local and systemic toxicity is common, especially following long continuous use on large areas of damaged skin, in flexures or with polythene occlusion. If used in children or on the face courses should be limited to 5 days. Long-term continuous therapy should be avoided in all patients irrespective of age. Occlusion must not be used. Topical corticosteroids may be hazardous in psoriasis for a number of reasons, including rebound relapses following development of tolerance, risk of generalised pustular psoriasis and local systemic toxicity due to impaired barrier function of the skin. Careful patient supervision is important.

General: systemic absorption of topical corticosteroids can produce reversible HPA-axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment. Patients receiving a large dose of a potent topical steroid applied to a large surface area should be evaluated periodically for evidence of HPA-axis suppression. If HPA-axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application or to substitute a less potent corticosteroid. Recovery of HPA-axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids. Any of the side effects that are reported following systemic use of corticosteroids, including adrenal suppression, may also occur with topical corticosteroids, especially in infants and children. Paediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. If irritation develops, treatment should be discontinued and appropriate therapy instituted. Betamethasone is not for ophthalmic use. Visual disturbance may be reported with systemic and topical (including intranasal, inhaled and intraocular) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, they should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances,

which may include cataract, glaucoma or rare diseases such as CSCR which have been reported after use of systemic and topical corticosteroids.

Paediatric population: paediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA-axis suppression and to exogenous corticosteroid-induced HPA-axis suppression and to exogenous corticosteroid effects than adult patients because of greater absorption due to a larger skin surface area to body weight ratio. HPA-axis suppression, Cushing's syndrome and intracranial hypertension have been reported in paediatric patients receiving topical corticosteroids. Manifestations of adrenal suppression in paediatric patients include linear growth retardation, delayed weight gain, low plasma cortisol levels and an absence of response to ACTH stimulation. Manifestations of intracranial hypertension include a bulging fontanelle, headaches and bilateral papilledema. Therefore, topical steroids should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus (according to the SmPC of some registered topical betamethasone preparations it is not recommended to use it during pregnancy).

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): betamethasone skin preparations are generally well tolerated and side effects are rare. The systemic absorption of betamethasone may be increased if extensive body surface areas or skin folds are treated for prolonged periods or with excessive amounts of steroids. Suitable precautions should be taken in these circumstances, particularly with infants and children. Local adverse reactions that have been reported with the use of betamethasone: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, striae and miliaria. Continuous application without interruption may result in local atrophy of the skin, striae and superficial vascular dilation, particularly on the face. Blurred vision has been reported with corticosteroid use (frequency not known). Children who use betamethasone topically may have an increased risk of side effects including slowed growth and delayed weight gain.

2.2 Indirect risks (incorrect use): excessive prolonged use of topical corticosteroids can suppress pituitary-adrenal functions resulting in secondary adrenal insufficiency, which is usually reversible. In such cases appropriate symptomatic treatment is indicated. If HPA-axis suppression is noted, an attempt should be made to withdraw the drug, reduce the frequency of application or to substitute a less potent steroid. The steroid content of each tube is so low as to have little or no toxic effect in the unlikely event of accidental oral ingestion.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	POM					
AT	List I					
BE	POM					
BiH	POM					
CH	List II					
CZ	POM					
DE	POM					
EE	POM					
ES	POM					
FI	POM					
FR	List I					
GE	Not subject to prescription					

HR	List I					
HU	POM					
IE	List II					
IT	List II					
LT	POM					
LV	POM					
MK	POM					
NL	POM					
PL	POM					
PT	POM					
RO	List I					
RS	POM					
SE	POM					
SI	POM					
UK	POM					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, as applicable): Proposed recommendation: **List I**

Criteria: continuous application of corticosteroids without interruption may result in local atrophy of the skin, striae and superficial vascular dilation, particularly on the face. Excessive prolonged use of topical corticosteroids can suppress pituitary-adrenal functions resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease.

3.2.2 Paediatric use: dosage in children should be limited to 5 days. Physician supervision needed.

3.2.3 Social dimension: the introduction of topical steroids of varying potency has rendered the therapy of inflammatory cutaneous disorders more effective and less time-consuming. The usefulness of these may lead to drug abuse.

4. REFERENCES/COMMENTS

4.1 References: Melclass database: https://melclass.edqm.eu/

Macedonian Agency for Medicinal Products and Medical Devices (MALMED): https://lekovi.zdravstvo.gov.mk/drugsregister/overview

MHRA: http://www.mhra.gov.uk/spc-pil/

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluclorolone

1.2 ATC code: D07AC02

1.3 Therapeutic indications: eczema and dermatitis, e.g. atopic eczema, seborrhoeic eczema, discoid eczema, otitis externa, contact dermatitis, neurodermatitis, lichen planus, discoid lupus erythematosus.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: https://www.vademecum.es/equivalencia-lista-cutanit+ultra+crema+0.2%25-espana-d07ac02-es_1

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Desoximetasone

1.2 ATC code: D07AC03

1.3 Therapeutic indications: indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

1.4 Posology and duration of treatment: a thin film of desoximetasone ointment to be applied (rub in gently) to the affected skin areas twice daily.

1.5 Pharmaceutical forms: cream 0.05%-0.25%, ointment 0.25%

1.6 Contraindications: it is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

1.7 Relevant warnings: systemic absorption of topical corticosteroids can produce reversible HPA-axis suppression with the potential for clinical glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of the topical corticosteroid. Because of the potential for systemic absorption, use of topical corticosteroids may require that patients be periodically evaluated for HPA-axis suppression. Factors that predispose patients using a topical corticosteroid to HPA-axis suppression include the use of more potent steroids, use over large surface areas, use over prolonged periods, use under occlusion, use on an altered skin barrier and use in patients with liver failure. An ACTH stimulation test may be helpful in evaluating patients for HPA-axis suppression. If HPA-axis suppression is documented, an attempt should be made to gradually withdraw the drug, to reduce the frequency of application or to substitute a less potent steroid. Manifestations of adrenal insufficiency may require supplemental systemic corticosteroids. Recovery of HPA-axis function is generally prompt and complete upon discontinuation of topical corticosteroids. Cushing's syndrome, hyperglycaemia and unmasking of latent diabetes mellitus can also result from systemic absorption of topical corticosteroids. Use of more than one corticosteroid-containing product at the same time may increase the total systemic corticosteroid exposure. Paediatric patients may be more susceptible to systemic toxicity from use of topical corticosteroids.

Local adverse reactions may be more likely to occur with occlusive use, prolonged use or use of higher potency corticosteroids. Reactions may include atrophy, striae, telangiectasias, burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection and miliaria. Some local adverse reactions may be irreversible.

Allergic contact dermatitis to any component of topical corticosteroids is usually diagnosed by a failure to heal rather than a clinical exacerbation. Clinical diagnosis of allergic contact dermatitis can be confirmed by patch testing.

Concomitant skin infections should be treated with an appropriate antimicrobial agent. If the infection persists, the medication should be discontinued until the infection has been adequately treated.

Paediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA-axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio. Desoximetasone should not be used in children under 1 year of age.

2.1 Direct risks (pharmacovigilance): the following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae and miliaria.

2.2 Indirect risks (incorrect use): topically applied corticosteroids can be absorbed in sufficient amounts and produce systemic effects.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	Not authorised					
AT	Not authorised					
BE	Not authorised					
BiH	Not authorised					
CH	Not authorised					
CZ	Not authorised					
EE	Not authorised					
ES	Not authorised					
FI	POM					
FR	Not authorised					
GE	Not authorised					
HR	Not authorised					
HU	Not authorised					
IE	Not authorised					
IT	List II					
LT	Not authorised					
LV	Not authorised					
MK	Not authorised					
NL	POM					
PL	Not authorised					
PT	Not authorised					
RO	Not authorised					
RS	POM					
SE	Not authorised					
SI	Not authorised					
UK	Not authorised					

No more data available from other member states.

Melclass database[1]: Currently not available

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, as applicable): Proposed recommendation: **List I**

Criteria: continuous application of corticosteroids without interruption may result in local atrophy of the skin, striae and superficial vascular dilation, particularly on the face. Excessive prolonged use of topical corticosteroids can suppress pituitary-adrenal functions resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease.

3.2.2 Paediatric use: desoximetasone should not be used in children under 1 year of age.

3.2.3 Social dimension: -

[1]Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

4. REFERENCES/COMMENTS

4.1 References: DailyMed: https://dailymed.nlm.nih.gov/dailymed/

RxList: https://www.rxlist.com/desoximetasone-generic-drug.htm#warnings

ALIMS: https://www.alims.gov.rs/latin/lekovi/pretrazivanje-humanih-lekova/

Melclass database: https://melclass.edqm.eu/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluocinolone Acetonide

1.2 ATC code: D07AC04

1.3 Therapeutic indications: treating a wide variety of inflammatory, pruritic and allergic disorders of the skin. Eczema and dermatitis: atopic eczema, seborrhoeic eczema, discoid eczema, otitis externa, contact dermatitis, neurodermatitis. Prurigo. Psoriasis (excluding widespread plaque psoriasis). Lichen planus. Discoid lupus erythematosus.

The lower strengths of fluocinolone acetonide (0.0025% w/w and 0.00625% w/w) are indicated for milder forms of these conditions; for maintenance therapy when control has been achieved with fluocinolone acetonide for use under occlusive dressings; and for paediatric dermatology e.g. infantile eczema.

1.4 Posology and duration of treatment: adults (including the elderly) and children above 1 year of age: topical administration: a small quantity of cream or ointment is applied lightly to the affected area two or three times a day and massaged gently and thoroughly into the skin. When an occlusive dressing is required, the affected area should first be thoroughly cleansed. Cream or ointment is then applied and covered with a suitable dressing. Occlusion should not be used for children or for the face. The cream is particularly suitable for moist and weeping surfaces and for flexures of the body. The ointment is suitable for dry scaly lesions.

Fluocinolone acetonide gel: a small quantity of gel is massaged into the scalp night and morning using the fingertips. For maintenance therapy, treatment should be repeated once or twice weekly.

1.5 Pharmaceutical forms: cream, ointment, gel, topical solution (0.01%, 0.025% w/w, 0.0025% w/w, 0.00625% w/w).

1.6 Contraindications: primary infections of the skin caused by bacteria, fungi or viruses and in rosacea, acne, perioral dermatitis, anogenital pruritus and napkin eruption. Fluocinolone acetonide should not be used in patients that are hypersensitive to any of the ingredients. Fluocinolone acetonide preparations are not advised in the treatment of children under 1 year of age.

1.7 Relevant warnings: long-term continuous steroid therapy can produce local atrophic skin changes and dilatation of the superficial blood vessels, particularly when occlusive dressings are used or when skin folds are involved. Prolonged use of topical steroids or treatment of extensive areas, even without occlusion, can result in sufficient absorption of the steroid to produce the features of hypercorticalism and underlying adrenal suppression, especially in infants and children. It is recommended that treatment on the face and for children should not normally be extended beyond 5 days, and occlusion in such cases should not be used. When there is an infection associated with an inflammatory skin condition, fluocinolone acetonide should only be administered if adequate anti-infective cover is given. When using topical steroids to treat psoriasis there are risks both of rebound relapse following the development of tolerance, and of generalised pustular psoriasis. Impairment of the barrier function of the skin may lead to local and systemic toxicity. Careful patient supervision is important. Treatment should be discontinued if unfavourable reactions are seen. The eyes should be avoided.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): Immune system disorders: local hypersensitivity reactions.

Skin and subcutaneous tissue disorders: dermatitis, perioral dermatitis acne or worsening of acne, rosacea. Extensive treatment, particularly involving occlusive dressings or where skin folds are involved, can result in both local atrophic changes, such as striae, skin thinning and telangiectasia. Mild depigmentation, which may be reversible, hypertrichosis and irreversible striae.

Endocrine disorders: adrenal suppression.

General disorders and administration site conditions: irritation at the site of application, infections and

infestations. The use of topical steroids on infected lesions without the addition of appropriate anti-infective therapy can result in the spread of opportunist infections.

2.2 Indirect risks (incorrect use): accidental ingestion: if greater quantities are ingested and toxicity develops, symptomatic treatment should be given.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	Not authorised					
AT	Not authorised					
BE	Not authorised					
BiH	POM					
CH	Not authorised					
CZ	POM					
DE	POM					
EE	Not authorised					
ES	POM					
FI	Not authorised					
FR	List I					
GE	Not authorised					
HR	Not authorised					
HU	POM					
IE	Not authorised					
IT	List II					
LT	POM					
LV	POM					
MK	POM					
NL	Not authorised					
PL	POM					
PT	POM					
RO	List I					
RS	POM					
SE	POM					
SI	POM					
UK	POM					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, as applicable): Proposed recommendation: **List I**

Criteria: continuous application of corticosteroids without interruption may result in local atrophy of the

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

skin, striae and superficial vascular dilation, particularly on the face. Excessive prolonged use of topical corticosteroids can suppress pituitary-adrenal functions resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease.

3.2.2 Paediatric use: dosage in children should be limited to 5 days. Physician supervision needed.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Melclass database: https://melclass.edqm.eu/

MALMED: https://lekovi.zdravstvo.gov.mk/drugsregister/overview

MHRA: http://www.mhra.gov.uk/spc-pil/

Electronic Medicines Compendium (EMC): https://www.medicines.org.uk

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluocortolone

1.2 ATC code: D07AC05

1.3 Therapeutic indications: all skin diseases which respond to topical corticoid therapy, e.g. contact dermatitis; contact eczema; occupational eczema; vulgar, nummular, degenerative and seborrheic eczema; dyshidrotic eczema; eczema in varicose syndrome (but not directly onto lower limb ulcers); anal eczema; eczema in children; neurodermatitis (endogenous eczema, atopic dermatitis); psoriasis; lichen ruber planus et verrucosus; lupus erythematosus discoides; first degree burns; sunburn; insect bites.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are only authorised in Italy (legal status: List II) and Spain (legal status: POM)).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable):

Proposed recommendation: based on the available data, medicines containing this active substance are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: http://www.shijiebiaopin.net/upload/product

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Diflucortolone

1.2 ATC code: D07AC06

1.3 Therapeutic indications: for the topical treatment of corticoid-responsive dermatoses that are unresponsive to less potent corticosteroids and in the absence of infection.

1.4 Posology and duration of treatment: Adults: initially, diflucortolone should be applied thinly twice daily. When the condition improves or when longer periods of treatment are required one application daily is appropriate. Long-term continuous therapy with topical corticosteroids should be avoided, with a usual maximum duration of 4 weeks. If used on the face, courses should be limited to 5 days and occlusion should not be used.

Children 1-4 years of age: diflucortolone should be applied thinly twice daily. It should be used with great care, for short periods and generally only on the advice of a doctor specialising in dermatology. Courses should be limited to 5 days and occlusion should not be used.

Children 5 years of age and over: initially, diflucortolone should be applied thinly twice daily. When the condition improves one application daily is appropriate. Courses should be limited to 1-2 weeks. If used on the face, courses should be limited to 5 days and occlusion should not be used.

Diflucortolone should not be used in children under 1 year of age.

Elderly: natural thinning of the skin occurs in the elderly.

Occlusive dressings: an occlusive dressing may be called for in unusually refractory cases and usually under specialist supervision. If an infection develops under the dressing, occlusive treatment must be terminated.

The cream is suitable for weeping skin conditions. In weeping skin diseases it allows secretions to drain away, thus providing for rapid reduction of swelling and drying up of the skin. The cream is also suitable for application to moist, exposed and hairy areas of the body. If the skin dries out too much under protracted use of cream, the patient should be switched to a form which contains more fat oily cream or ointment.

1.5 Pharmaceutical forms: cream 0.1%-0.3% and ointment 0.1%-0.3%

1.6 Contraindications: rosacea and perioral dermatitis. Acne vulgaris, undiagnosed perianal and genital pruritus, napkin eruptions, viral infections, primary bacterial or fungal infections of the skin. Secondary infections in the absence of appropriate anti-infective therapy. Post-vaccination skin reactions in the area to be treated. Diflucortolone is not suitable for the treatment of ophthalmic conditions. Hypersensitivity to the active substances or to any of the excipients

1.7 Relevant warnings: long-term continuous therapy with topical corticosteroids should be avoided, with a usual maximum duration of 3-4 weeks irrespective of age. Adrenal suppression can occur, even without occlusion. If used on children up to the age of 4 years or on the face, courses should be limited to 5 days and occlusion should not be used. Diflucortolone may be applied under an occlusive dressing. Each dressing should not be left on for more than 24 hours. Although occlusive dressings may be used repeatedly, it should be noted that systemic corticoid absorption is likely to be increased with a consequent increased risk of adrenal suppression. If occlusive treatment is expected to be prolonged, it is advisable to change the dressing every 12 hours. Diflucortolone should not be allowed to come into contact with the eyes. Topical corticosteroids may be hazardous in psoriasis for a number of reasons, including rebound relapses following development of tolerance, risk of generalised pustular psoriasis and local and systemic toxicity due to impaired barrier function of the skin. Careful patient supervision is important in psoriasis. Exacerbation of skin infections may occur. Infections or secondarily infected dermatoses require additional therapy with antibiotics or chemotherapeutic agents. This treatment can often be topical, but for heavy infections systemic antibacterial therapy may be necessary. If fungal infections are present, a topically active antimycotic should be applied. If aggravation of skin irritation develops with the use of

diflucortolone, treatment should be withdrawn and appropriate therapy installed. Allergic contact dermatitis due to topical corticosteroids and excipients can occur. In these cases eczema fails to improve or deteriorates with treatment. Corticosteroid hypersensitivity occurs most frequently among patients with stasis dermatitis and leg ulceration. Such an observation should be corroborated with appropriate diagnostic patch testing. The appropriate corticosteroid concentration and the choice of the vehicle is crucial in detecting corticosteroid hypersensitivity in patch tests. Patients with an allergy to corticosteroids may cross-react to several corticosteroids to which they have not previously been exposed. After topical application, allergies to cross-reacting systemically applied corticosteroids may occur. As known from systemic corticoids, glaucoma may also develop by using local corticoids (e.g. after large-dose or extensive application over a prolonged period, occlusive dressing technique or application to the skin around the eyes).

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): common local adverse reactions reported with diflucortolone formulations in clinical studies include burning, pruritus, erythema and irritations. In common with all other topical corticoids, side effects may occur when diflucortolone is applied to large areas of the body (10% or more) and for long periods of time (more than 4 weeks), especially if the ointment or an occlusive dressing is being used. There may be local signs such as atrophy of the skin, telangiectasia, striae, acneiform changes, perioral dermatitis and hypertrichosis, or systemic corticoid effects caused by absorption. Systemic absorption can produce the features of hypercorticism. Therefore, caution should be exercised when using occlusive dressings, as there is a possibility that natural steroid production may be suppressed. In rare cases, allergic skin reactions may occur.

2.2 Indirect risks (incorrect use): on the basis of results from acute toxicity studies with diflucortolone preparations, no acute risk of intoxication is to be expected either after a single dermal application of an overdose (application over a large area under conditions favouring resorption).

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AMI	Not authorised					
AT	List I					
BE	Not authorised					
BiH	POM					
CH	Not authorised					
CZ	Not authorised					
EE	POM					
ES	POM					
FI	Not authorised					
FR	List I					
GE	Not authorised					
HR	Not authorised					
HU	Not authorised					
IE	Not authorised					
IT	List II					
LT	Not authorised					
LV	Not authorised					
MK	POM					
NL	Not authorised					

PL	Not authorised					
PT	POM					
RO	POM					
RS	Not authorised					
SE	Not authorised					
SI	Not authorised					
UK	POM					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, as applicable): Proposed recommendation: **List I**

Criteria: continuous application of corticosteroids without interruption may result in local atrophy of the skin, striae and superficial vascular dilation, particularly on the face. Excessive prolonged use of topical corticosteroids can suppress pituitary-adrenal functions resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease.

3.2.2 Paediatric use: diflucortolone should not be used in children under 1 year of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: MALMED: https://lekovi.zdravstvo.gov.mk/drugsregister/overview

MHRA: http://www.mhra.gov.uk/spc-pil/

Melclass database: https://www.medicines.org.uk

4.2 Comments: -

[1]Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fludroxycortide

1.2 ATC code: D07AC07

1.3 Therapeutic indications: adults and children: eczema and dermatitis of all types including childhood and adult atopic eczema, photodermatitis, primary irritant and allergic dermatitis, lichen planus, lichen simplex, prurigo nodularis, discoid lupus erythematosus, necrobiosis lipoidica, pretibial myxoedema and erythroderma.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Dailymed: https://dailymed.nlm.nih.gov/dailymed/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluocinonide

1.2 ATC code: D07AC08

1.3 Therapeutic indications: fluocinonide is suitable for treating a wide variety of local inflammatory, pruritic and allergic disorders of the skin. It is indicated in the following conditions: eczema and dermatitis: atopic eczema, seborrheic dermatitis, discoid eczema, contact dermatitis, neurodermatitis. Prurigo, psoriasis (excluding widespread plaque psoriasis). Lichen planus. Discoid lupus erythematosus. Fluocinonide ointment with its emollient effects is particularly suitable for dry scaly lesions.

1.4 Posology and duration of treatment: it is recommended that fluocinonide is used undiluted.

Adults: a small quantity of fluocinonide should be applied three to four times daily to the affected area and massaged well in. Once improvement is apparent, usage may be reduced to twice or even once daily.

Fluocinonide preparations are not advised in the treatment of children under 1 year of age. Over 1 year: As adult dose; however it is recommended that treatment should not normally be extended beyond 5 days and occlusion should not be used in such cases.

Elderly: to be used as adult dose.

1.5 Pharmaceutical forms: Cream 0.05% w/w, ointment 0.05% w/w, cream 0.1%.

1.6 Contraindications: contraindicated in rosacea, acne and perioral dermatitis. As with all topical steroids, it is contraindicated in tuberculous, syphilitic, fungal and viral infections of the skin. The product should not be used for napkin eruption or anogenital pruritus.

1.7 Relevant warnings: long-term continuous topical steroid therapy can produce atrophic skin changes and dilation of the superficial blood vessels particularly when occlusive dressings are used or where skin folds are involved. Prolonged use of topical steroids or treatment of extensive areas, even without occlusion, can result in sufficient absorption of the steroid to produce the features of hypercorticalism and underlying adrenal suppression, especially in infants and children. It is recommended that treatment on the face should not normally be extended beyond 5 days, and occlusion should not be used in such cases. Where there is bacterial infection associated with an inflammatory skin condition, fluocinonide should only be administered if adequate antibacterial cover is also given. When using topical steroids to treat psoriasis there are risks of rebound relapse following the development of tolerance, and of generalised pustular psoriasis. Impairment of the barrier function of the skin may lead to local and systemic toxicity. Careful patient supervision is important. Treatment should be discontinued if unfavourable reactions are seen. Absorption is greatest where the skin is thin or raw.

Pregnancy: there is inadequate evidence of safety in human pregnancy. Topical administration of steroids to pregnant animals can cause abnormalities of foetal development, including cleft palate and intrauterine growth retardation. There may therefore be a very small risk of such effects on the human foetus.

Lactation: topical steroids should not be applied to the breasts prior to nursing. When topical steroid treatment is considered necessary for other parts of the body, both the amount applied and the length of treatment should be minimised.

2.1 Direct risks (pharmacovigilance): side effects are extremely rare but, as with all topical steroids, the occasional patient may show an adverse reaction such as hypersensitivity. Irritation at the site of application may occur infrequently. Extensive treatment, particularly involving occlusive dressings or where skin folds are involved, can result in both local atrophic changes, such as striae, skin thinning and telangiectasia, and systemic effects such as adrenal suppression. The use of topical steroids on infected lesions, without the addition of appropriate anti-infective therapy, can result in the spread of opportunist infection. The eyes should be avoided. Local side effects include contact dermatitis, perioral dermatitis, acne, or worsening of acne or acne rosacea, mild depigmentation which may be reversible and hypertrichosis.

2.2 Indirect risks (incorrect use): toxic effects are not likely to occur following accidental ingestion. Similarly, the components of the vehicles, singly or collectively, have not been shown to produce toxic effects in these quantities.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	Not authorised					
AT	Not authorised					
BE	Not authorised					
BiH	Not authorised					
CH	List II					
CZ	Not authorised					
EE	Not authorised					
ES	POM					
FI	Not authorised					
FR	Not authorised					
GE	Not authorised					
HR	Not authorised					
HU	Not authorised					
IE	Not authorised					
IT	List II					
LT	Not authorised					
LV	Not authorised					
MK	Not authorised					
NL	Not authorised					
PL	Not authorised					
PT	Not authorised					
RO	Not authorised					
RS	Not authorised					
SE	Not authorised					
SI	Not authorised					
UK	POM					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, as applicable): Proposed recommendation: **List I**

Criteria: long-term continuous topical steroid therapy can produce atrophic skin changes and dilation of the superficial blood vessels particularly when occlusive dressings are used or where skin folds are involved. Excessive prolonged use of topical corticosteroids can suppress pituitary-adrenal functions resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease.

[1]Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

3.2.2 Paediatric use: not to be used in children under 1 year of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: MHRA: http://www.mhra.gov.uk/spc-pil/ and EMC: https://www.medicines.org.uk

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Budesonide

1.2 ATC code: D07AC09

1.3 Therapeutic indications: relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are only authorised in Italy (legal status: List II)).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, medicines containing this active substance are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Target Pharma HealthCare: www.targetpharma.gr/en/product/budesonide

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Diflorasone

1.2 ATC code: D07AC10

1.3 Therapeutic indications: relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are only authorised in Spain (legal status: POM)).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, medicines containing this active substance are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: RxList: https://www.rxlist.com/florone-drug.htm

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Amcinonide

1.2 ATC code: D07AC11

1.3 Therapeutic indications: for the treatment of acute and chronic dermatoses sensitive to corticosteroids, such as atopic dermatitis, contact dermatitis, eczematous dermatoses, psoriasis and neurodermatitis.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are only authorised in Belgium (legal status: POM) and Germany (legal status: POM)).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, medicines containing this active substance are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: sDrugs.com: https://www.sdrugs.com/?c=drug&s=amciderm

Mutual Recognition Information (MRI) Index: https://mri.cts-mrp.eu/Human/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Halometasone

1.2 ATC code: D07AC12

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: MRI Index: https://mri.cts-mrp.eu/Human/ and Melclass database: https://melclass.edqm.eu/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Mometasone

1.2 ATC code: D07AC13

1.3 Therapeutic indications: for the symptomatic treatment of inflammatory and pruritic skin conditions which respond to external treatment with glucocorticoids, such as atopic dermatitis and psoriasis (excluding widespread plaque psoriasis).

1.4 Posology and duration of treatment: adults, including older people and children aged 2 years and over: a thin film of mometasone should be applied to the affected skin area once daily. Strong topical corticosteroids generally should not be applied to children or to the face without close monitoring by the physician. The amount applied should be limited to the least amount compatible with an effective therapeutic regimen and duration of the treatment should be no longer than 5 days. Mometasone should not be used for long periods (over 3 weeks) or on large areas (over 20% of body surface area). In children a maximum of 10% of body surface area should be treated. Use of a weaker corticosteroid is often advisable when there is a clinical improvement.

Paediatric population: children below 2 years: mometasone is a potent group III glucocorticoid. It is not recommended for use in children below 2 years due to insufficient data on safety.

1.5 Pharmaceutical forms: ointment 0.01%; cream 0.01%; cutaneous solution 0.01%; cutaneous emulsion 0.01%

1.6 Contraindications: hypersensitivity to the active substance, other corticosteroids. Mometasone is contraindicated in facial rosacea, acne vulgaris, skin atrophy, perioral dermatitis, perianal and genital pruritis, napkin eruptions, bacterial (e.g. impetigo, pyodermas), viral (e.g. herpes simplex, herpes zoster, chickenpox, verrucae vulgaris, condyloma acuminata, molluscum contagiosum), parasitical and fungal (e.g. candida or dermatophyte) infections, varicella, tuberculosis, syphilis or post-vaccine reactions. Mometasone should not be used on wounds or on skin, which is ulcerated.

1.7 Relevant warnings: if irritation or sensitisation develop with the use of mometasone, treatment should be withdrawn and appropriate therapy instituted. Should an infection develop, use of an appropriate antifungal or antibacterial agent should be instituted. If a favourable response does not occur promptly, the corticosteroid should be discontinued until the infection is adequately controlled. Systemic absorption of topical corticosteroids can produce reversible HPA-axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycaemia and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment. Patients applying a topical steroid to a large surface area or areas under occlusion should be evaluated periodically for evidence of HPA-axis suppression. Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as CSCR which have been reported after use of systemic and topical corticosteroids. Any of the side effects that are reported following systemic use of corticosteroids, including adrenal suppression, may also occur with topical corticosteroids, especially in infants and children.

Paediatric population: paediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. As the safety and efficacy of mometasone fin paediatric patients below 2 years of age have not been established, mometasone is not recommended in this age group. Mometasone may be used with caution in paediatric patients 2 years of age or older, although the safety and efficacy of the use of mometasone for longer than 3 weeks have not been established. Local and systemic toxicity is common especially following long continued use on large areas of damaged skin, in flexures and with polythene occlusion. If used in childhood, or on the face, occlusion should not be used. If used on the face, courses should be limited to 5 days. Long-term continuous therapy should be avoided in all patients irrespective of age.

Topical steroids may be hazardous in psoriasis for a number of reasons including rebound relapses following development of tolerance, risk of centralised pustular psoriasis and development of local or

systemic toxicity due to impaired barrier function of the skin. If used in psoriasis careful patient supervision is important. If topical treatment with potent glucocorticoids is stopped, a rebound phenomenon can develop which takes the form of a dermatitis with intense redness, stinging and burning. This can be prevented by slow reduction of the treatment, for instance continue treatment on an intermittent basis before discontinuing treatment. Glucocorticoids can change the appearance of some lesions and make it difficult to establish an adequate diagnosis and can also delay the healing. Mometasone is not for ophthalmic use (including the eyelids) because of the very rare risk of glaucoma simplex or subcapsular cataract.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance):

Infections and infestations	
Very rare	Folliculitis
Not known	Infection, furuncle
Nervous system disorders	
Very rare	Burning sensation
Not known	Paraesthesia
Eye disorders	
Not known	Blurred vision
Skin and subcutaneous tissue disorders	
Common	Tingling, stinging sensation
Uncommon	Formation of papules, pustules
Very rare	Pruritus
Not known	Dermatitis contact, skin hypopigmentation, hypertrichosis, skin striae, dermatitis acneiform, skin atrophy
General disorders and administration site conditions	
Not known	Application site pain, application site reactions

Local adverse reactions reported infrequently with topical dermatologic corticosteroids include dry skin, skin irritation, perioral dermatitis, dermatitis, skin maceration, miliaria and telangiectasia.

Paediatric population: paediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced hypothalamic-pituitary-adrenal axis suppression and Cushing's syndrome than mature patients because of a larger skin surface to body weight ratio. Chronic corticosteroid therapy may interfere with the growth and development of children.

2.2 Indirect risks (incorrect use): excessive prolonged use of topical corticosteroids can suppress hypothalamic-pituitary-adrenal function resulting in secondary adrenal insufficiency which is usually reversible. Reasonable symptomatic treatment should be initiated. If necessary, problems with the electrolyte balance must be treated. If HPA-axis 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. The steroid content of each container is so low as to have little or no toxic effect in the unlikely event of accidental oral ingestion.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	POM					
AT	List I					
BE	POM					

BiH	POM					
BG	POM					
CH	List II					
CZ	POM					
DE	POM					
EE	POM					
ES	POM					
FI	POM					
FR	List I					
HR	List I					
HU	POM					
IE	List II					
IT	List II					
LT	POM					
LV	POM					
MK	POM					
NL	POM					
PL	POM					
PT	POM					
RO	List II					
RS	POM					
SK	POM					
SE	POM					
SI	POM					
UK	POM					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: manifestations of Cushing's syndrome, hyperglycaemia and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment. Patients applying a topical steroid to a large surface area or areas under occlusion should be evaluated periodically for evidence of HPA-axis suppression.

3.2.2 Paediatric use: as the safety and efficacy of mometasone in paediatric patients below 2 years of age have not been established, mometasone is not recommended in this age group. Mometasone may be used with caution in paediatric patients of 2 years of age or older, although the safety and efficacy of the use of mometasone for longer than 3 weeks have not been established.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: HPRA: https://www.hpra.ie

State Medicines Control Agency of Lithuania: https://www.vvkt.lt

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

MRI Index: https://mri.cts-mrp.eu/Human/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Methylprednisolone Aceponate

1.2 ATC code: D07AC14

1.3 Therapeutic indications: for the topical treatment of moderate to severe inflammatory skin conditions such as atopic dermatitis (endogenous eczema, neurodermatitis), contact eczema, degenerative or dyshidrotic eczema, simple eczema.

1.4 Posology and duration of treatment: the product should be applied thinly once per day to the affected areas of skin. In general, the duration of use should not exceed 12 weeks in adults and 4 weeks in children. The safety of methylprednisolone aceponate in children under 3 years has not been established.

1.5 Pharmaceutical forms: cutaneous emulsion 0.1%; cream 0.1%; ointment 0.1%; cutaneous solution 0.1%.

1.6 Contraindications: known hypersensitivity to the active ingredient. Primary bacterial, viral and fungal diseases of the skin and secondarily infected eczemas or intertrigo acne, perioral dermatitis, rosacea, atrophic skin diseases and vaccination skin reactions in the area to be treated and, in general, should not be used on weeping surfaces.

1.7 Relevant warnings: glucocorticoids must only be used at as low a dose as possible, especially in children, and only for as long as is absolutely necessary to achieve and maintain the desired therapeutic effect. Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions, which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and administration of appropriate therapy. Local skin infections can be potentiated by topical glucocorticoid use. Care must be taken when using methylprednisolone aceponate to avoid contact with the eyes, deep open wounds and mucosae. Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes, which may include cataract, glaucoma or rare diseases such as CSCR which have been reported after use of systemic and topical corticosteroids. No impairment of adrenocortical function has been observed in children on large-area (40-60% of the skin surface) or even occlusive treatment with methylprednisolone aceponate. After application of methylprednisolone aceponate to 60% skin surface area under occlusive conditions for 22 hours, suppression of plasma cortisol levels and influence on circadian rhythm was observed in adult healthy volunteers. Extensive application of topical corticosteroids to large areas of the body or for prolonged periods of time, in particular under occlusion, significantly increases the risk of side effects. Treatment under occlusive conditions should be avoided unless indicated. Note that diapers/nappies as well as intertriginous areas might represent occlusive conditions. When treating large areas of skin, the duration of treatment should be kept as short as possible as the possibility of absorption or a systemic effect cannot be completely excluded. As with all other glucocorticoids unprofessional use can mask clinical symptomatology. As known from systemic corticoids, glaucoma may also develop from using local corticoids (e.g. after large-dose or extensive application over a prolonged period, occlusive dressing techniques or application to the skin around the eyes).

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): in clinical studies, most frequently observed side effects included application site burning and application site pruritus with cream and ointment. For fatty ointment, application site folliculitis and application site burning were observed most frequently. As with other corticoids for topical application, the following local side effects may occur in rare cases: skin atrophy, skin striae, application site folliculitis, hypertrichosis, telangiectasia, perioral dermatitis, skin discoloration and allergic skin reactions to one of the ingredients of the formulations. Systemic effects due to absorption may occur when topical preparations containing corticoids are applied.

2.2 Indirect risks (incorrect use): results from acute toxicity studies do not indicate that any risk of acute

intoxication is to be expected following a single dermal application of an overdose (application over a large area under conditions favourable to absorption) or unintentional oral ingestion.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	POM					
AT	List I					
BE	POM					
BiH	Not authorised					
BG	POM					
CH	List II					
CZ	POM					
DE	POM					
EE	POM					
ES	POM					
FI	POM					
FR	Not authorised					
GE	Not subject to prescription					
HR	List I					
HU	POM					
IE	List II					
IT	Not authorised					
LT	POM					
LV	POM					
MK	POM					
NL	Not authorised					
PL	POM					
PT	POM					
RO	List I					
RS	Not authorised					
SE	Not authorised					
SI	POM					
UK	Not authorised					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term use and medical supervision required.

3.2.2 Paediatric use: the safety in infants below the age of 4 months has not been established. Therefore,

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

methylprednisolone aceponate should not be used under occlusive conditions. It is mportant to note that diapers can be occlusive. A careful benefit/risk assessment is needed in the case of children aged between 4 months and 3 years.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: State Medicines Control Agency of Lithuania: https://www.vvkt.lt

Melclass database: https://melclass.edqm.eu

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Beclometasone

1.2 ATC code: D07AC15

1.3 Therapeutic indications: for the treatment of the various forms of eczema in children and adults including atopic and discoid eczemas; primary irritant and allergic dermatitis; psoriasis (excluding widespread plaque psoriasis); neurodermatoses including lichen simplex; intertrigo; discoid lupus erythematosus. The cream is often appropriate for moist or weeping surfaces and the ointment for dry, lichenified or scaly lesions but this is not invariably so.

1.4 Posology and duration of treatment: beclometasone should be applied thinly over the whole of the affected area and gently rubbed in. Initially, application should be made twice daily, but when improvement is seen, the intervals between applications may be extended and treatment eventually stopped. If no improvement is seen within 2 to 4 weeks, reassessment of the diagnosis or referral may be necessary. After cessation of treatment, should the condition recur, twice daily treatment should be re-instituted. However, when improvement is seen again, the intervals between applications may be gradually extended until maintenance dosing of application every third or fourth day is achieved. This is likely to avoid subsequent reappearance of the condition. The beneficial effects may be enhanced by preliminary use of hot soaks, or by intermittent applications or occlusive dressings.

1.5 Pharmaceutical forms: 0.25 mg/g cream and 0.25 mg/g ointment.

1.6 Contraindications: the cream should not be applied to the eyes. Rosacea, acne vulgaris, perioral dermatitis. Primary cutaneous viral infections (e.g. herpes simplex, chickenpox). Hypersensitivity to the preparation. Varicose ulcers or any other stasis ulcers. Use of beclometasone is not indicated in the treatment of primarily infected skin lesions caused by infection with fungi (e.g. candidiasis, tinea) or bacteria (e.g. impetigo); primary or secondary infections due to yeasts; perianal and genital pruritus; dermatoses in children under 1 year of age, including dermatitis and napkin eruptions

1.7 Relevant warnings: long-term continuous therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion. The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis, discoid lupus erythematosus and severe eczema. If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result. If used in childhood, or on the face, courses should be limited if possible to 5 days and occlusion should not be used. Topical corticosteroids may be hazardous in psoriasis for a number of reasons including rebound relapses, development of tolerance, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin. If used in psoriasis careful patient supervision is important. Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and systemic administration of antimicrobial agents. Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressings, and so the skin should be cleansed before a fresh dressing is applied.

Fire hazard in contact with dressings clothing and bedding: patients should be instructed not to smoke or go near naked flames because of risks of severe burns. Fabric (clothing, bedding, dressings, etc.) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): prolonged and intensive treatment with highly active corticosteroid preparations may cause local atrophic changes in the skin such as thinning, striae and dilatation of the superficial blood vessels, particularly when occlusive dressings are used or when skin folds are involved. As with other topical corticosteroids, prolonged used of large amounts, or treatment of extensive areas, can result in sufficient systemic absorption to produce the features of hypercorticism. The effect is more likely to occur in infants and children, and if occlusive dressings are used. In infants,

the napkin may act as an occlusive dressing. Should systemic corticosteroid effects arise from application of beclometasone, topical treatment should be discontinued. If adrenal function is impaired the patient will need to be protected from any harmful effects of stress with oral corticosteroid preparations until normal adrenal function is established. There are reports of pigmentation changes and hypertrichosis with topical steroids. In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease (see precautions). Beclometasone is usually well tolerated, but if signs of hypersensitivity appear, application should stop immediately. Exacerbation of symptoms may occur.

2.2 Indirect risks (incorrect use): if systemic corticosteroid effects arise from application of beclometasone, topical treatment should be discontinued. If adrenal function is impaired, the patient will need to be protected from any harmful effects of stress with oral corticosteroid preparations until normal adrenal function is established.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	Not authorised					
AT	Not authorised					
BE	Not authorised					
BiH	Not authorised					
BG	Not authorised					
CH	Not authorised					
CZ	Not authorised					
DE	Not authorised					
EE	Not authorised					
ES	POM					
FI	Not authorised					
FR	Not authorised					
GE	Not authorised					
HR	Not authorised					
HU	Not authorised					
IE	Not authorised					
IT	List II					
LT	Not authorised					
LV	Not authorised					
MK	Not authorised					
NL	Not authorised					
PL	Not authorised					
PT	Not authorised					
RO	Not authorised					
RS	Not authorised					
SE	Not authorised					
SI	Not authorised					
UK	POM					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term use and medical supervision required.

3.2.2 Paediatric use: it should not be used to treat dermatoses in children under 1 year of age, including dermatitis and napkin eruptions.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Melclass database: https://melclass.edqm.eu

MHRA: http://www.mhra.gov.uk/spc-pil/

MRI Index: https://mri.cts-mrp.eu/Human/

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Hydrocortisone Aceponate

1.2 ATC code: D07AC16

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are authorised only in Spain (legal status: POM)).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, medicines containing this active substance are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: MRI Index: https://mri.cts-mrp.eu/Human/ and Melclass database: https://melclass.edqm.eu/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluticasone

1.2 ATC code: D07AC17

1.3 Therapeutic indications: fluticasone propionate is a potent topical corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses; these include the following: atopic dermatitis, nummular dermatitis (discoid eczemas), prurigo nodularis, psoriasis (excluding widespread plaque psoriasis), lichen simplex chronicus (neurodermatitis) and lichen planus, seborrhoeic dermatitis, irritant or allergic contact dermatitis, discoid lupus erythematosus, an adjunct to systemic steroid therapy in generalised erythroderma, insect bite reactions, miliaria (prickly heat).

Children: for children and infants aged 3 months and over who are unresponsive to lower potency corticosteroids, fluticasone is indicated for the relief of the inflammatory and pruritic manifestations of atopic dermatitis under the supervision of a specialist. Expert opinion should be sought prior to the use of fluticasone in other corticosteroid-responsive dermatoses in children.

1.4 Posology and duration of treatment: adults, elderly, children and infants aged 3 months and over. Apply thinly and gently rub in using only enough to cover the entire affected area once or twice a day for up to 4 weeks until improvement occurs, then reduce the frequency of application or change the treatment to a less potent preparation. Allow adequate time for absorption after each application before applying an emollient. Therapy with topical corticosteroids should be gradually discontinued once control is achieved and an emollient continued as maintenance therapy. Rebound of pre-existing dermatoses can occur with abrupt discontinuation of topical steroids especially with potent preparations.

Duration of treatment for adults and elderly: if the condition worsens or does not improve within 4 weeks, treatment and diagnosis should be re-evaluated.

Children over 3 months: children are more likely to develop local and systemic side effects of topical corticosteroids and, in general, require shorter courses and less potent agents than adults. Care should be taken when using fluticasone propionate to ensure the amount applied is the minimum that provides therapeutic benefit.

Duration of treatment for children and Infants: when fluticasone is used in the treatment of children, if there is no improvement within 7-14 days, treatment should be withdrawn and the child re-evaluated. Once the condition has been controlled (usually within 7-14 days), frequency of application should be reduced to the lowest effective dose for the shortest possible time. Continuous daily treatment for longer than 4 weeks is not recommended.

Elderly: clinical studies have not identified differences in responses between the elderly and younger patients. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption occurs. Therefore, the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

Renal/Hepatic Impairment: in case of systemic absorption (when application is over a large surface area for a prolonged period), metabolism and elimination may be delayed therefore increasing the risk of systemic toxicity. Therefore, the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

1.5 Pharmaceutical forms: cream 0.05% and ointment 0.05%.

1.6 Contraindications: hypersensitivity to the active substance. The following conditions should not be treated with fluticasone propionate: untreated cutaneous infections, rosacea, acne vulgaris, perioral dermatitis, perianal and genital pruritus, pruritus without inflammation, dermatoses in infants under 3 months of age, including dermatitis and nappy rash.

1.7 Relevant warnings: fluticasone propionate should be used with caution in patients with a history of local hypersensitivity to other corticosteroids. Local hypersensitivity reactions may resemble

symptoms of the condition under treatment. Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamic pituitary-adrenal (HPA) axis suppression, leading to glucocorticosteroid insufficiency, can occur in some individuals as a result of increased systemic absorption of topical steroids. If either of the above are observed, withdraw the drug gradually by reducing the frequency of application or by substituting a less potent corticosteroid. Abrupt withdrawal of treatment may result in glucocorticosteroid insufficiency. Risk factors for increased systemic effects are: potency and formulation of topical steroid; duration of exposure; application to a large surface area; use on occluded areas of skin (e.g. on intertriginous areas or under occlusive dressings (in infants the nappy may act as an occlusive dressing); increasing hydration of the stratum corneum; use on thin skin areas such as the face; use on broken skin or other conditions where the skin barrier may be impaired; in comparison with adults, children and infants may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic adverse effects. This is because children have an immature skin barrier and a greater surface area to body weight ratio compared with adults.

Children: in infants and children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression is more likely to occur.

Use in psoriasis: topical steroids should be used with caution in psoriasis as rebound relapses, development of tolerance, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin have been reported in some cases. If used in psoriasis, careful patient supervision is important.

Application to the face: prolonged application to the face is undesirable as this area is more susceptible to atrophic changes.

Application to the eyelids: if applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as cataract and glaucoma might result from repeated exposure.

Visual disturbance: visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, they should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as CSCR which have been reported after use of systemic and topical corticosteroids.

Concomitant infection: appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and administration of appropriate antimicrobial therapy.

Infection risk with occlusion: bacterial infection is encouraged by the warm, moist conditions within skin folds or caused by occlusive dressings. When using occlusive dressings, the skin should be cleansed before a fresh dressing is applied.

Chronic leg ulcers: topical corticosteroids are sometimes used to treat the dermatitis around chronic leg ulcers. However, this use may be associated with a higher occurrence of local hypersensitivity reactions and an increased risk of local infection. Overt suppression of the HPA-axis (morning plasma cortisol less than 5 micrograms/dL) is very unlikely to result from therapeutic use of fluticasone propionate cream or ointment unless treating more than 50% of an adult's body surface and applying more than 20 g per day.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): Infections and infestations: very rare: opportunistic infection.

Immune system disorders: very rare: hypersensitivity.

Endocrine disorders: very rare: hypothalamic, HPA-axis suppression: weight gain/obesity; slowing down of children's weight gain/growth; Cushingoid symptoms (e.g. lunar face, central obesity); decrease in endogenous cortisol levels; hyperglycaemia/glycosuria; hypertension; osteoporosis; cataracts; glaucoma.

Skin and subcutaneous tissue disorders: common: itching; uncommon: localised skin burning sensation; very rare: skin flushing, atrophy, stretch marks, telangiectasia, changes in pigmentation, hair growth, allergic contact dermatitis, exacerbation of existing symptoms, pustular psoriasis, redness, rash, urticaria.

Eye disorders: frequency not known: blurred vision.

2.2 Indirect risks (incorrect use): symptoms and signs: topical administration of fluticasone propionate may result in systemic exposure. The likelihood of an acute overdose is very low, but signs of chronic overdose or misuse may lead to signs of excessive cortisol concentration.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	Not authorised					
AT	Not authorised					
BE	POM					
BiH	Not authorised					
BG	Not authorised					
CH	List II					
CZ	Not authorised					
DE	POM					
EE	POM					
ES	POM					
FI	Not authorised					
FR	Not authorised					
GE	Not authorised					
HR	Not authorised					
HU	POM					
IE	Not authorised					
IT	List II					
LT	POM					
LV	POM					
MK	Not authorised					
NL	POM					
PL	POM					
PT	POM					
RO	POM					
RS	Not authorised					
SE	POM					
SI	Not authorised					
UK	POM					

No more data available from other member states.

Melclass database: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: pharmacological profile, short-term treatment and medical supervision required.

3.2.2 Paediatric use: in infants and children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression is more likely to occur. Children over 3 months are more likely to develop local and systemic side effects of topical corticosteroids and, in general, require shorter courses and less potent agents than adults. Care should be taken when using fluticasone propionate to ensure the amount applied is the minimum that provides therapeutic benefit.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Melclass database: https://melclass.edqm.eu

MHRA: http://www.mhra.gov.uk/spc-pil/

MRI Index: https://mri.cts-mrp.eu/Human/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Prednicarbate

1.2 ATC code: D07AC18

1.3 Therapeutic indications: prednicarbate is a medium-potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

1.4 Posology and duration of treatment: a thin film should be applied and gently rubbed in to the affected skin areas twice daily. Prednicarbate may be used in paediatric patients 1 year of age or older. Safety and efficacy in paediatric patients for more than 3 weeks of use have not been established. Use in paediatric patients under 1 year of age is not recommended. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary. It should not be used with occlusive dressings unless directed by the physician. Prednicarbate should not be applied in the diaper area if the child still requires diapers or plastic pants as these garments may constitute occlusive dressing.

1.5 Pharmaceutical forms: cream 0.1% and ointment 0.1% - 0.25%

1.6 Contraindications: hypersensitivity to the active substance.

1.7 Relevant warnings: systemic absorption of topical corticosteroids can produce reversible HPA-axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycaemia and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment. Patients applying a topical steroid to a large surface area or under occlusion should be evaluated periodically for evidence of HPA-axis suppression. This may be done by using the ACTH stimulation, early morning (AM) plasma cortisol and urinary free cortisol tests. Prednicarbate did not produce significant HPA-axis suppression when used at a dose of 30 g/day for a week in 10 adult patients with extensive psoriasis or atopic dermatitis. Prednicarbate did not produce HPA-axis suppression in any of 59 paediatric patients with extensive atopic dermatitis when applied BID for 3 weeks to > 20% of the body surface. If HPA-axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of the application or to substitute a less potent corticosteroid. 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. Paediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. If irritation develops, use of prednicarbate should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing a failure to heal rather than noting a clinical exacerbation, as observed with most topical products not containing corticosteroids. If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial agent should be used. If a favourable response does not occur promptly, use of prednicarbate should be discontinued until the infection has been adequately controlled.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): the following local adverse reactions are reported: less common: burning, itching, drying, scaling or cracking of the skin; irritation of the skin; pain; raised, dark red or wart-like spots on the skin, especially when used on the face; shininess or thinness of the skin; thinning of the skin with easy bruising, especially when used on the face or where the skin folds together (e.g. between the fingers). Rare: blistering, burning, crusting, dryness or flaking of the skin; burning, crawling, itching, numbness, prickling, "pins and needles" or tingling feelings; hives or welts; itching, scaling, severe redness, soreness or swelling of the skin; skin rash. Not known: irritation of the skin around the mouth; redness and scaling around the mouth.

Some side effects of prednicarbate may occur that usually do not need medical attention. Advice by the healthcare professional should be given if the following side effects continue or are bothersome: not known: acne or pimples; burning and itching of the skin with pinhead-sized red blisters; burning, itching and pain in hairy areas or pus at the root of the hair; increased hair growth on the forehead, back, arms

and legs; lightening of normal skin colour; lightening of the treated areas of dark skin; reddish purple lines on the arms, face, legs, trunk or groin.

2.2 Indirect risks (incorrect use): an overdose of prednicarbate for cutaneous use is not expected to produce life-threatening symptoms. However, long-term use of high steroid doses can lead to symptoms such as thinning skin, easy bruising, changes in the shape or location of body fat (especially in the face, neck, back and waist), increased acne or facial hair, menstrual problems, impotence or loss of interest in sex.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	Not authorised					
AT	Not authorised					
BE	Not authorised					
BiH	Not authorised					
BG	Not authorised					
CH	List II					
CZ	Not authorised					
DE	POM					
EE	Not authorised					
ES	POM					
FI	Not authorised					
FR	Not authorised					
GE	Not authorised					
HR	Not authorised					
HU	Not authorised					
IE	Not authorised					
IT	List II					
LT	Not authorised					
LV	Not authorised					
MK	Not authorised					
NL	Not authorised					
PL	Not authorised					
PT	Not authorised					
RO	Not authorised					
RS	Not authorised					
SE	Not authorised					
SI	Not authorised					
UK	Not authorised					

No more data available from other member states.

Melclass database[1]: Classification currently available

3.2 Social dimension of classification:

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: short-term use and medical supervision required.

3.2.2 Paediatric use: prednicarbate may be used with caution in paediatric patients 1 year of age or older. The safety and efficacy of use for longer than 3 weeks in this population have not been established. Since safety and efficacy of prednicarbate have not been established in paediatric patients below 1 year of age, its use in this age group is not recommended

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Melclass database: https://melclass.edqm.eu and Drugs.com: https://www.drugs.com/mtm/prednicarbate-topical.html

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Difluprednate

1.2 ATC code: D07AC19

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: MRI Index: https://mri.cts-mrp.eu/Human/ and Melclass database: https://melclass.edqm.eu/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Ulobetasol

1.2 ATC code: D07AC21

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: MRI Index: https://mri.cts-mrp.eu/Human/ and Melclass database: https://melclass.edqm.eu/

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Clobetasol

1.2 ATC code: D07AD01

1.3 Therapeutic indications: clobetasol is a very potent topical corticosteroid indicated for adults, elderly and children over 1 year for the relief of the inflammatory and pruritic manifestations of steroid-responsive dermatoses. These include the following: psoriasis (excluding widespread plaque psoriasis), recalcitrant dermatoses, lichen planus, discoid lupus erythematosus and other skin conditions which do not respond satisfactorily to less potent steroids.

1.4 Posology and duration of treatment: a small amount should be applied to the affected area once or twice a day. Treatment must be stopped once the condition is under control. Stopping clobetasol abruptly can cause return of the original condition. If the condition worsens or does not improve within 2-4 weeks, treatment and diagnosis should be re-evaluated. Treatment should not be continued for more than 4 weeks without checking the patient's condition. If continuous treatment with a corticosteroid is considered necessary, a less potent preparation should be considered. In very resistant lesions, especially where there is hyperkeratosis, the anti-inflammatory effect of clobetasol can be enhanced, if necessary, by occluding the treated area with polyethylene film. Overnight occlusion is usually adequate to attain a satisfactory response. Thereafter improvement can be maintained by application without occlusion.

Paediatric population: clobetasol is contraindicated in children under 1 year of age. Long-term treatment should be avoided in children.

1.5 Pharmaceutical forms: cream 0.05%; ointment 0.05%; cutaneous foam 0.05%; shampoo 0.05%; cutaneous solution 0.05%.

1.6 Contraindications: hypersensitivity to the active substance, rosacea, acne vulgaris, perioral dermatitis, primary viral skin infections (e.g. herpes simplex, chickenpox), perianal and genital pruritus, skin lesions primarily infected by fungi (e.g. candidiasis, tinea) or bacteria (e.g. impetigo), dermatoses in children under the age of 1, including dermatitis and nappy rash.

1.7 Relevant warnings: continued long-term treatment must be avoided when possible, especially in children, since it may cause adrenal suppression even without occlusion. If clobetasol is needed for use in children, weekly review of treatment is recommended. After prolonged treatment with strong topical corticosteroids, the face and, to a lesser extent, other parts of the body may exhibit atrophic changes. This must be kept in mind when treating conditions such as psoriasis, discoid lupus erythematosus and severe eczema. If clobetasol is applied to the eyelids, care is needed to ensure that the preparation does not enter the eyes since it may lead to glaucoma. If clobetasol comes into contact with the eyes, the affected area must be washed with an abundant amount of water. The use of topical steroids in the treatment of psoriasis may carry a risk for a number of reasons, including rebound relapses, development of tolerance, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin. If used to treat psoriasis, careful patient supervision is important. Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions that have become infected. Any spread of infections requires withdrawal of topical corticosteroid therapy and systemic administration of antimicrobial agents. Bacterial infection is favoured by the warm, moist conditions induced by occlusive dressings, so the skin should be cleansed before a fresh dressing is applied. It must be kept in mind that nappies can act as an occlusive dressing. The gradual withdrawal of prolonged treatments is recommended.

Visual disturbance: visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as CSCR which have been reported after use of systemic and topical corticosteroids.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): the most common adverse reactions during the treatment are skin disorders such as pruritus and local skin burning. Prolonged treatment could cause athropic changes (uncommon). Adrenal suppression may occur very rarely, mainly associated with long-term treatment.

Infections and infestations: very rare: opportunistic infection.

Immune system disorders: very rare: hypersensitivity, generalised rash.

Endocrine disorders: very rare: HPA-axis suppression, Cushingoid features: (e.g. moon face, central obesity), increased weight/obesity, delayed weight gain/growth retardation in children, decreased endogenous cortisol levels, hyperglycaemia/glucosuria, hypertension, osteoporosis, cataract, glaucoma, alopecia, trichorrhexis.

Skin and subcutaneous tissue disorders: common: pruritus, local skin burning/skin pain; uncommon: skin atrophy*, striae*, telangiectasias*; very rare: skin thinning*, skin wrinkling*, skin dryness*, pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, allergic contact dermatitis/dermatitis, pustular psoriasis, erythema, rash, urticaria.

General disorders and administration site conditions: very rare: application site irritation/pain.

Eye disorders: not known: vision, blurred.

*Skin features secondary to local and/or systemic effects of HPA-axis suppression. Prolonged use of large amounts of corticosteroids, or treatment of extensive areas, can result in sufficient systemic absorption to produce the features of hypercortisolism. This effect is more likely to occur in infants and children, and if occlusive dressings are used. In infants, the napkin may act as an occlusive dressing.

2.2 Indirect risks (incorrect use): acute overdose is very unlikely to occur; however, in the event of chronic overdose or misuse, signs of Cushing's syndrome may appear in which case the application of topical steroids must be stopped gradually due to the risk of adrenal insufficiency.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:

Country	Classification	Indications	MS	MDD	MQP	Additional Info
AM	POM					
AT	List I					
BE	POM					
BiH	POM					
BG	POM					
CH	List II					
CZ	POM					
DE	POM					
EE	POM					
ES	POM					
FI	POM					
FR	List I					
HR	Not authorised					
HU	POM					
IE	List II					
IT	List II					
LT	POM					

LV	POM					
MK	Not authorised					
NL	POM					
PL	POM					
PT	POM					
RO	POM					
RS	Not authorised					
SE	POM					
SI	Not authorised					
UK	POM					

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: **List I**

Criteria: pharmacological profile, short-term use and medical supervision required.

3.2.2 Paediatric use: clobetasol is contraindicated in children under 1 year of age. Children are more likely to develop local and systemic side effects of topical corticosteroids and in general require shorter courses and less potent agents than adults. Courses should be limited if possible to several days and reviewed weekly.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Melclass database: https://melclass.edqm.eu

MHRA: http://www.mhra.gov.uk/spc-pil/

MRI Index: https://mri.cts-mrp.eu/Human/

4.2 Comments: -

[1] Available at: https://melclass.edqm.eu/ (NB: this is the CD-P-PH/PHO's recommendation at the moment of the compilation of the evidence-based review)

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Halcinonide

1.2 ATC code: D07AD02

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states).

3.2 Social dimension of classification:

3.2.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable): Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: MRI Index: https://mri.cts-mrp.eu/Human/ and Melclass database: https://melclass.edqm.eu/

4.2 Comments: -

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