**Department of Biological Standardisation,**
**European Network of Official Medicines Control Laboratories &HealthCare (DBO)**

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

Report classification/justification of

- Antibiotics and chemotherapeutics for dermatological use (medicines belonging to the ATC group D06)

- Racecadotril (ATC code: A07XA04)

**Table of Contents**

## INTRODUCTION

**The legal classification of medicines as regards their supply with or without a medical prescription has implications for patient safety, patient accessibility to medicines and the responsible management of healthcare expenditure.**

For a long time, the **Council of Europe** (**which is distinct from the European Union**)[1] has been concerned with the supply conditions of medicines for human use and the harmonisation of national legal provisions from the perspective of patient safety and public health protection. An initial Recommendation AP(61)2 was drawn up in 1961 to control a growing tendency of misuse and overuse of sedative and narcotic medicines by empowering the competent authorities to classify new medicines into prescription and non-prescription medicines, considering the risks associated with the active substance and the conditions of use of the medicines.

On 12 April 2007, the Council of Europe Committee of Ministers adopted Resolution ResAP (2007)1 on the classification of medicines as regards their supply[2]. The resolution is aimed at promoting patient safety and improving patient accessibility to medicines, and is focused on public health. The resolution:

> "*1. Recommends to the governments of the member states of the Partial Agreement in the Social and Public Health Field that they supply information on the national legal classification of medicines as regards their supply on a regular basis;*
>
> *2. Recommends to the same governments that they apply the general provisions and the classification of active substances depending on the supply conditions of the medicines which contain them,* ***as set out in the appendices***."

The text of this Council of Europe resolution comprises a recommendation of the Committee of Ministers (Foreign Affairs Ministers, representing the governments of states participating in an activity) to member states to implement the stipulations of the resolution into national legislation or to adapt national legislation.

Although recommendations are not legally binding, they are legal instruments; they may create soft law and contain a political statement. The Committee of Ministers may also invite the member states to report on their efforts to implement a recommendation.

It has to be borne in mind that the decisions of Committee of Experts on the classification of medicines as regards their supply (CD-P-PH/PHO) concerning the supply of medications with or without a medical prescription take into account national assessments and scientific rationale. Revisions are completed and made available following each second annual meeting of the CD-P-PH/PHO.

The annually revised appendices of the Council of Europe Resolution ResAP (2007)1 on the classification of medicines as regards their supply are a relevant reference for the European pharmaceutical industry, as well. In particular, industry is impacted if national authorities implement the revisions, as applicable.

The classification criteria set out in the Council of Europe resolutions have been included in **European Union** legislation, such as Directive 92/26/EC and Directive 2001/83/EC (art. 70-75). In particular, 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*

[1] www.coe.int
[2] http://go.edqm.eu/ResAP20071

*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]."

To date, the classification of medicines remains a competency of states in Europe. This also holds true for the member states of the European Union.

The CD-P-PH/PHO, which is co-ordinated by the European Directorate for the Quality of Medicines & HealthCare (EDQM, Council of Europe), does not issue recommendations on the classification of particular medicines, but on **active substances used in a medicine for a specific therapeutic purpose**. The CD-P-PH/PHO reviews the classification of medicines (INN/ATC[4]) authorised in Europe via national and European marketing authorisation procedures (the latter is applicable to the 47 Council of Europe member states, including the European Union member states) in order to establish recommendations for the classification of medicines and their supply conditions (see also Glossary of Terms, page 7), involving:

- Medicines that have not yet been included in Council of Europe recommendations;

- Medicines that qualify to be released from prescription status, i.e. a switch to "over the counter" (OTC) status or vice-versa;

- Revisions of current classifications.

The CD-P-PH/PHO meets twice annually to finalise the annual review of the recommendations and appendices of ResAP (2007)1. The review is completed at the second of these meetings and is published on the website of the EDQM. These recommendations are an integral part of the Council of Europe's Committee of Ministers Resolution ResAP (2007)1 on the classification of medicines as regards their supply.

The Committee of Experts does not give advice relating to pending marketing authorisation procedures. It uses scientific approaches and methods (taking into account the pharmacological properties of the medicines), and considers issues relating to direct and indirect risks (pharmacovigilance), as well as misuse/abuse and matters of public health concern.

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[5]. The Commission of the European Union is entitled to participate in the meetings of the CD-P-PH/PHO.

[3] http://goo.gl/Uy22V1
[4] INN: International non-proprietary name; ATC: Anatomical Therapeutic Chemical (ATC) classification
[5] http://www.whocc.no/atc_ddd_index/

## 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 conclusions of the reports arising from reviews of scientific classifications of medicines and the rationale and debates on which the recommendations on the classification of medicines as regards their supply, taken by the CD-P-PH/PHO at its 2012-2013 meetings, were based. The document was reviewed and endorsed by the CD-P-PH/PHO at its 56th meeting on 11-12 March 2014.

**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

| | |
|---|---|
| ADR | Adverse drug reaction |
| ATC | Anatomical Therapeutic Chemical[6] |
| MS | Maximal strength |
| MDD | Maximal daily dose |
| MQP | Maximal quantity per pack |
| OTC | Over-the-counter<br>(medicine supplied without prescription) |
| PDR | Physician's Desk Reference (www.pdr.net/) |
| POM | Prescription only medicine |
| SmPC | Summary of product characteristics |

### Classification used throughout this document

Following the stipulations of Resolution ResAP (2007)1, the medicine contains one or more active substances classified as **List I** or **List II** to which the following criteria apply:

***List I***
The supply of a medicine containing one of the substances on this list may only be repeated if the prescriber specifies so on the prescription;

***List II***
The supply of a medicine containing one of the substances on this list may be repeated without the prescriber having specified so, provided that he/she did not explicitly forbid such repetition and that the amount supplied at renewals (and their frequency) be consistent with medical and pharmaceutical data (such as the prescribed daily dose, the duration of treatment, the degree of medical supervision required by the condition, etc.);

***Exemptions from Lists I and II***
- For certain substances, exemptions from the "prescription only" requirement may appear in Lists I and II:
    - In respect of a low dosage or concentration of the active substances and/or therapeutic indications of the medicines in which they are contained;
    - According to the route of administration and the composition of the medicine;
    - According to the total content of the medicine per container.

- Active substances classified according to the conditions of supply of the medicines which contain them as supplied without prescription, i.e. OTC medicines.

***Medicines not subject to prescription (OTC medicines)***
Active substances of medicines that are classified as not subject to prescription according to the criteria given in item 4 of the General Provisions of ResAP (2007)1 are classified in the list "Medicines not subject to prescription (OTC medicines)".

For the purpose of this resolution, OTC medicines are understood to be those also having a valid marketing authorisation issued by a competent authority.

It is possible that a given active substance can be contained in both an OTC medicine and a medicine subject to prescription of the same ATC (Anatomical Therapeutic Chemical

[6] WHO Collaborating Centre for Drug Statistics Methodology - http://www.whocc.no/atc_ddd_index/

classification) because of the particular conditions of use of the medicines in question.

**General criteria for classification in the lists**

a. List I

*1.* 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;

*2.* Active substances of medicines administered for diagnostic purposes;

*3.* Active substances with a new pharmacological mechanism of action.

b. List II

Active substances of medicines indicated for conditions for which the patient may continue regular or intermittent treatment without new medical advice, and for which well-known undesirable effects do not call for frequent clinical examinations.

c. List of OTC medicines

(see previous page)

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Aciclovir

**1.2 ATC Code:** D06BB03 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** Adults and adolescents > 12 years: herpes simplex infections of the skin, including genital herpes and herpes labialis.

**1.4 Posology and duration of treatment:** As early as possible, following onset of signs and symptoms, 5 - 6 times daily for periods of 5 to 10 days.

**1.5 Pharmaceutical forms:** 5% cream.

**1.6 Contraindications (SmPC):** Hypersensitivity to aciclovir.

**1.7 Relevant warnings (SmPC):** Topical application of aciclovir, especially to genital lesions, may sometimes produce transient stinging, burning, itching or erythema. It should not be applied to the eye. Absorption of aciclovir is usually slight after topical application to intact skin, although this may be increased by changes in formulation.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** General: oedema and/or pain at the application site. Skin: pruritus, rash.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (1) + Exemption Annex III | Cutaneous use | Adults and children > 12 years; short treatment (no longer than 10 days); treatment of herpes labialis (cold sores) | 5% | | 100mg |
| Publication** | I (1) + Exemption Annex III | Cutaneous use | Adults and children > 12 years; short treatment (no longer than 10 days); treatment of herpes labialis (cold sores) | 5% | | 100mg |
| Austria (A) | I (1) + Exemption Annex III | | | | | |
| Armenia (ARM) | Not authorised | | | | | |
| Belgium (B) | OTC see Annex III | | | | | |
| Bulgaria (BG) | II | | | | | |
| Bosnia and Herzegovina (BIH) | I | | | | | |
| Switzerland (CH) | I (1) + Exemption Annex III | | | | | |
| Czech Republic (CZ) | I + Exemption Annex III | | | | | |
| Germany (D) | II + Exemption Annex III | | | | | |
| Denmark (DK) | II + Exemption Annex III | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Spain (E) | II + Exemption Annex III | | | | | |
| France (F) | II + Exemption Annex III | | | | | |
| Finland (FIN) | II + Exemption Annex III | | | | | |
| Great Britain (GB) | II + Exemption Annex III | | | | | |
| Hungary (H) | II + Exemption Annex III | | | | | |
| Croatia (HR) | OTC see Annex III | | | | | |
| Italy (I) | II | | | | | |
| Ireland (IRL) | II + Exemption Annex III | | | | | |
| Lithuania (LT) | OTC see Annex III | | | | | |
| Latvia (LV) | OTC see Annex III | | | | | |
| Republic of Macedonia (MK) | I | | | | | |
| Norway (N) | II | | | | | |
| The Netherlands (NL) | OTC see Annex III | | | | | |
| Portugal (P) | II | | | | | |
| Poland (PL) | OTC see Annex III | | | | | |
| Romania (RO) | I | | | | | |
| Sweden (S) | OTC see Annex III | | | | | |
| Slovenia (SLO) | OTC see Annex III | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List 1 + Exemption Annex III**
*Exemptions:*

- Cutaneous use;
- Adults and children > 12 years;
- For short treatment of herpes labialis (cold sores);
- MS: 5%, MQP: 100mg.

**3.2 Paediatric use:** Not recommended in children < 12 years.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Aciclovir, combinations (combination: aciclovir 5% and hydrocortisone 1%)

**1.2 ATC Code:** D06BB53

**1.3 Therapeutic indications:** Treatment of early signs and symptoms of recurrent herpes labialis (cold sores) to reduce the progression of cold sore episodes to ulcerative lesions in immunocompetent adults and adolescents (12 years of age and older).

**1.4 Posology and duration of treatment:** It should be applied 5 times per day for 5 days (i.e. approximately every 3-4 hours omitting the night time application). Treatment should be initiated as early as possible, preferably immediately after the first signs or symptoms. A sufficient quantity of the cream should be applied each time to cover the affected area including the outer margin of the lesions, if present.
Treatment should be carried out for 5 days. If lesions are still present after 10 days, users should be advised to consult a doctor.

**1.5 Pharmaceutical forms:** Cream: aciclovir 5% and hydrocortisone 1%

**1.6 Contraindications (SmPC):** Hypersensitivity to the active substances, valaciclovir or to any of the excipients.

Use for skin lesions caused by any virus other than herpes simplex, or for fungal, bacterial or parasitic skin infections.

**1.7 Relevant warnings (SmPC):** For cutaneous use only: to be applied to lesions on the lips and face.
It is not recommended for application to mucous membranes (e.g.in the eye or inside the mouth or nose or on the genitals).
It should not be used to treat genital herpes.
Particular care should be taken to avoid contact with the eye.
In patients with severe recurrent herpes labialis, other underlying disease should be excluded. It should not be used with occlusive dressings, such as plasters or specialised cold sore patches/plasters.
It is not recommended for use by immunocompromised patients due to the possibility of pseudo-opportunistic infections or drug resistant strains which require systemic antiviral therapy.
Long-term continuous use should be avoided.
It should not be used for longer than 5 days.
Treatment of patients with concomitant dermatitis of other origin has not been studied.
It contains cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis), and propylene glycol which may cause skin irritation.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

### 2.1 Direct risks (Pharmacovigilance):

Adverse reactions:

*Skin and subcutaneous tissue disorders*
Common (≥1/100 to <1/10): drying or flaking of the skin
Uncommon (≥1/1,000 to <1/100): transient burning, tingling or stinging (following application of the product), itching.
Rare (≥ 1/10000 to <1/1000): erythema, pigmentation changes, application site reactions

including signs and symptoms of inflammation, contact dermatitis following application has been observed when applied under occlusion in dermal safety studies. Where sensitivity tests have been conducted, the reactive substance was hydrocortisone or a component of the cream base.

*Immune system disorders*
Very rare (<1/10000): Immediate hypersensitivity reactions including angioedema (based on post-marketing experience with single active acyclovir).

**2.1.1 Recent cases at European level: -**

**2.1.2 Indirect risks (incorrect use):** Prolonged or incorrect use may cause resistance to acyclovir or secondary infections. The systemic effect of glucocorticoids can occur in the event of increased absorption (e.g. when applied on large inflamed areas of skin, or on skin of which the stratum corneum of the epidermis is damaged). Occlusive bandages increase absorption.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

It is s a novel combination of well-known ingredients: aciclovir 5% and hydrocortisone 1%.

Aciclovir is an antiviral agent which is highly active in vitro against herpes simplex virus (HSV) types 1 and 2. Aciclovir is phosphorylated after entry into herpes infected cells to the active compound aciclovir triphosphate. The first step in this process is dependent on the presence of the HSV-coded enzyme thymidine kinase. Aciclovir triphosphate acts as an inhibitor of, and substrate for the herpes-specified DNA polymerase, preventing further viral DNA synthesis without affecting normal cellular processes.

Hydrocortisone is a mild corticosteroid that exerts a range of immunomodulatory effects. When applied topically, its primary role is to control various inflammatory skin disorders.

Such combination combines the antiviral activity of aciclovir and the anti-inflammatory action of hydrocortisone and reduces the progression of cold sore episodes into ulcerative lesions. The exact mechanism for this is not fully characterised, but is thought to be mediated through clearance of the virus and mitigating the local inflammatory response in the lip leading to lessening of the signs and symptoms.

Due to limited absorption, the systemic exposure of aciclovir is expected to be low following topical administration of aciclovir and hydrocortisone cream.

Glucocorticoids have the ability to penetrate stratum corneum of the epidermis and affect the deeper cell layers. Usually only a small proportion of the dose is absorbed, and it is thus not expected to affect the hormonal balance.

Data from the clinical studies does not show enhanced viral replication comparing to the aciclovir alone in healthy adults. No aciclovir resistant samples were identified during conducted clinical trials.

Adverse reactions seem to be comparable to those associated with aciclovir as mono-product.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | - | | | | | |
| Publication** | - | | | | | |
| A | I (1) | | | | | |
| B | I (1) | | | | | |
| CH | Not authorised | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| CZ | OTC see Annex III | | | | | |
| D | I | | | | | |
| DK | OTC see Annex III | | | | | |
| E | POM | | | | | |
| F | I | | | | | |
| FIN | I | | | | | |
| GB | I | | | | | |
| HR | Not authorised | | | | | |
| I | Not authorised | | | | | |
| IRL | Not authorised | | | | | |
| MK | Not authorised | | | | | |
| P | OTC see Annex III | | | | | |
| PL | OTC see Annex III | | | | | |
| SLO | OTC see Annex III | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation:** Only for combination products containing aciclovir 5% and hydrocortisone 1%: **List I + Exemption Annex III**
*Exemptions:*

- For cutaneous use;
- For short treatment (5 days) of early signs and symptoms of recurrent herpes labialis (cold sores);
- Immunocompetent adults and children > 12 years;
- MS: aciclovir 5% and hydrocortisone 1%;
- MQP: aciclovir 100 mg and hydrocortisone 20 mg in 2g pack.

*Criteria:*
Combination (first approval 07.2009, SE/H/882/01/DC) of well-established ingredients, with similar safety profile as for acyclovir alone and hydrocortisone alone products;
Easy self-diagnosis;
Need for early use;
Short time treatment (5 days);
Negligible increased systemic exposure.

**3.2 Paediatric use:** The safety profile in adolescents (12-17 years) was similar to that in adults. Not recommended in children < 12 years.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 37th edition.
FDA Medical Review Acyclovir 5% and hydrocortisone 1% - Xerese ® (Available at: http://goo.gl/nMShAv).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
Public Assessment Report Zoviduo cream (aciclovir 5% and hydrocortisone 1%) SE/H/882/01/DC (Available at: http://goo.gl/Tmfxqt).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Amikacin

**1.2 ATC Code:** D06AX12 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** No data (Martindale, PDR, EMC, *melclass*) concerning cutaneous use.

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: No data in *melclass* database.

**3.1 Conditions of supply (Indications, Administration Route, MS, MDD, MQP, as applicable):** No data (Martindale, PDR, *melclass* database) concerning topical skin use. No data from member states.

**Recommendation: Not to classify**

**3.2 Paediatric use:** -

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th and 37th editions.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Bacitracin; the zinc salt of bacitracin

**1.2 ATC Code:** D06AX05 Antibiotics for topical use, Other antibiotics for topical use

Combined preparations that contain neomycin and other antibiotics (e.g. bacitracin) are classified in D06AX04 – neomycin.

**1.3 Therapeutic indications:** First aid antibiotic to help prevent infection in minor cuts, scrapes and burns.

Bacitracin and bacitracin zinc are applied topically, often with other anti-bacterials such as neomycin and polymyxin B, and sometimes with corticosteroids, in the treatment of local infections due to susceptible organisms.

**1.4 Posology and duration of treatment:** 1 to 3 times daily.

**1 1.5 Pharmaceutical forms:** bacitracin zinc ointment 500 units/1g; combination products, ointments (bacitracin, neomycin, polymyxin B).

**1.6 Contraindications (SmPC):** Hypersensitivity to bacitracin, neomycin or other components.

*OTC (FDA OTC monograph part 333)*: "*Do not use in the eyes or apply over large areas of the body. Do not use if you are allergic to any of the ingredients. Do not use longer than 1 week unless directed by a doctor*."

**1.7 Relevant warnings (SmPC):** Hypersensitivity reactions, including rashes and anaphylaxis, have occurred with both systemic, and more rarely, with topical use.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Absorption from open wounds and from the bladder or peritoneal cavity may lead to adverse effects, although the dose-limiting toxicity of combined preparations is considered to be due to neomycin.

**2.1.1 Recent cases at European level:** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Use on deep or puncture wounds, animal bites or serious burns may lead to adverse effects due to absorption.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Bacitracin interferes with bacterial cell wall synthesis by blocking the function of the lipid carrier molecule that transfers cell wall sub-units across the cell membrane. It is active against many Gram-positive bacteria including staphylococci, streptococci (particularly group A streptococci) and clostridia. It is also active against *Actinomyces*, *Treponema pallidum* and some Gram-negative species such as *Neisseria* and *Haemophilus influenzae*, although most Gram-negative organisms are resistant.
Acquired bacterial resistance to bacitracin rarely occurs, but resistant strains of staphylococci have been detected.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | Currently not available | | | | | |
| Publication** | Currently not available | | | | | |
| A | Not authorised as mono-product | | | | | |
| ARM | Not authorised | | | | | |
| B | Not authorised as mono-product | | | | | |
| CH | Not authorised | | | | | |
| CZ | Not authorised as mono-product | | | | | |
| D | OTC see Annex III | | | | | |
| E | I | | | | | |
| F | I | | | | | |
| FIN | Not authorised as mono-product | | | | | |
| GB | Not authorised as mono-product | | | | | |
| H | II | | | | | |
| HR | Not authorised as mono-product | | | | | |
| MK | Not authorised as mono-product | | | | | |
| N | OTC see Annex III | | | | | |
| NL | II | | | | | |
| P | OTC see Annex III | | | | | |
| PL | Not authorised as mono-product | | | | | |
| RO | Not authorised as mono-product | | | | | |
| SLO | II | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

Available as a combination product in some member states.

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

**Recommendation: Not to classify as mono-product**

Combined preparations that contain neomycin and other antibiotics (e.g. bacitracin) are classified in D06AX04 – neomycin.

**Recommendation for combination products: List I + Exemption Annex III**
*Exemptions:*

- For cutaneous use;
- No longer than 7 days;
- Adults and children > 12 years;
- Not for large surfaces.

### 3.2 Paediatric use: -

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Chloramphenicol

**1.2 ATC Code:** D06AX02 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** Treatment of skin infections.

**1.4 Posology and duration of treatment:** 3 times daily.

**1.5 Pharmaceutical forms:** 1% ointment, 2% ointment.

**1.6 Contraindications (SmPC):** Hypersensitivity to chloramphenicol.

**1.7 Relevant warnings (SmPC):** Not recommended during pregnancy and breast-feeding.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Warnings: skin rashes and irritation after long-term use can cause *Saccharomyces* super-infections. Bone marrow hypoplasia, including aplastic anaemia and death, has been reported following local application of chloramphenicol.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (1) | | | | | |
| Publication** | I (1) | | | | | |
| A | Not authorised | | | | | |
| B | OTC see Annex III | | | | | |
| CZ | Not authorised | | | | | |
| D | II | | | | | |
| E | II | | | | | |
| F | - | | | | | |
| FIN | II | | | | | |
| HR | Not authorised | | | | | |
| LV | OTC see Annex III | Cutaneous | Purulent lesions | | | |
| MK | I | | | | | |
| P | Withdrawn in 2012 | | | | | |
| PL | I | | | | | |
| RO | Not authorised | | | | | |
| S | II | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I (1)**

*Criteria:*
Long-term use can cause *Saccharomyces* super-infections.
Bone marrow hypoplasia, including aplastic anaemia and death, has been reported following local application of chloramphenicol.

**3.2 Paediatric use:** No data available.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th and 37th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Chlortetracycline

**1.2 ATC Code:** D06AA02 Antibiotics for topical use, Tetracycline and derivatives

**1.3 Therapeutic indications:** Purulent skin infections; purulent burns and frostbite complications; mild inflammatory acne and as an adjunct to systemic treatment of more severe forms of rosacea (long-term treatment).
It may be used alone or with one or more other medicines that are applied to the skin.

**1.4 Posology and duration of treatment:** One or two times daily.

**1.5 Pharmaceutical forms:** 3% ointment.

**1.6 Contraindications (SmPC):** Hypersensitivity to chlortetracycline or any tetracycline; children < 12 years; pregnancy; lactation.

**1.7 Relevant warnings (SmPC):** Topical use carries the risk of sensitisation and may contribute to the development of resistance. Systemic treatment appears to produce better results.
Phototoxic reactions can occur in individuals using chlortetracycline, which are characterised by severe burns resulting from direct exposure of exposed surfaces to sunlight during therapy with chlortetracycline. Patients exposed to direct sunlight or ultraviolet light (artificial sunlight) should be advised that this reaction can occur, and treatment should be discontinued at the first evidence of erythema of the skin.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** It can cause photo-sensitivity, possible super-infections by *Saccharomyces* or other resistant strains, scalded skin syndrome (rarely), or pain, redness, swelling or other signs of irritation not present before use of this medicine.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** The use of drugs of the tetracycline class during tooth development may result in permanent discolouration of the teeth.
Chlortetracycline, like other tetracycline-class antibiotics, may cause foetal harm when administered during pregnancy, and may cause permanent discolouration of the teeth during development in children up to the age of 8 years. Teratogenicity following topical application cannot be excluded.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Chlortetracycline is a tetracycline derivative with uses similar to those of tetracycline. Chlortetracycline hydrochloride is used as a 1% ophthalmic ointment and as a 3% ointment for application to the skin. Chlortetracycline hydrochloride is a broad-spectrum antibiotic. It is active against a large number of gram-positive and gram-negative bacteria, including some that are resistant to penicillin. Topically-applied tetracycline preparations are not absorbed into the general circulatory system to any significant degree.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (1) | | | | | |
| Publication** | I (1) | | | | | |
| A | Not authorised | | | | | |
| B | Not authorised | | | | | |
| CH | Not authorised | | | | | |
| CZ | Not authorised | | | | | |
| D | II | | | | | |
| E | II | | | | | |
| F | I | | | | | |
| FIN | II | | | | | |
| HR | Not authorised | | | | | |
| HU | Not authorised | | | | | |
| GB | Not authorised | | | | | |
| I | Not authorised | | | | | |
| IRL | II | | | | | |
| LT | II | | | | | |
| MK | Not authorised | | | | | |
| N | II | | | | | |
| P | Not authorised | | | | | |
| PL | I | | | | | |
| RO | Not authorised | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I (1)**

*Criteria:*
Risk of sensitisation and may contribute to the development of resistance;
Possibility of super-infections of *Saccharomyces* or other resistant strains;
Possible hypersensitivity and cross-hypersensitivity reactions.

**3.2 Paediatric use:** Children > 12 years only.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Demeclocycline

**1.2 ATC Code:** D06AA01 Antibiotics for topical use, Tetracycline and derivatives

**1.3 Therapeutic indications:** Demeclocycline is administered orally in the hydrochloride form. No data concerning topical skin use is available.

**1.4 Posology and duration of treatment:** No data concerning topical skin use.

**1.5 Pharmaceutical forms:** Oral forms only.

**1.6 Contraindications (SmPC):** The same as for the tetracycline group (see pages 20; 49; 70).

**1.7 Relevant warnings:** -

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance): -**

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Demeclocycline is a tetracycline derivative, with uses similar to those of tetracycline. It is excreted more slowly by the body and effective blood concentrations are maintained for a longer period than tetracyclines.
Anti-microbial action is as for tetracycline. Demeclocycline is stated to be somewhat more active against certain strains of some organisms, including *Neisseria gonorrhoeae* and *Haemophilus influenzae*, as well as being the most active of the tetracyclines *in vitro* against *Brucella.*

Demeclocycline is administered orally in the hydrochloride form. No data concerning cutaneous use is available.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | Currently not available | | | | | |
| Publication** | Currently not available | | | | | |
| A | I (1) | | | | | |
| E | I | | | | | |
| PL | Not authorised | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

No data concerning cutaneous use is available.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** No data

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Docosanol

**1.2 ATC Code:** D06BB11 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** Treatment of early stages (prodromal or erythema phase) of recurrent labial herpes simplex infection (cold sores) in immuno-competent adults and adolescents (over 12 years old).

**1.4 Posology and duration of treatment:** *Adults and children >12 years*: Treatment must begin as soon as possible after the first cold sore symptoms or signs appear; 5 times daily; usually 4-6 days, no longer than 10 days.

**1.5 Pharmaceutical forms:** 10% cream.

**1.6 Contraindications (SmPC):** Hypersensitivity.

**1.7 Relevant warnings (SmPC):** Avoid application close to or in the eyes. The cream should not be used in immuno-compromised patients.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Nervous system disorders: headache. Adverse reactions at application site include dry skin, rashes and skin disorders.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Adverse reactions related to overdose by topical application of docosanol are unlikely because of negligible per-cutaneous absorption. Similarly, limited oral absorption makes the occurrence of adverse reactions unlikely following ingestion of docosanol.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | OTC see Annex III | | | | | |
| Publication** | OTC see Annex III | | | | | |
| A | OTC see Annex | | | | | |
| B | OTC see Annex III | | | | | |
| CZ | OTC see Annex III | | | | | |
| D | Not authorised | | | | | |
| F | OTC see Annex III | | | | | |
| HR | Not authorised | | | | | |
| I | Not authorised | | | | | |
| LV | OTC see Annex III | | | | | |
| MK | Not authorised | | | | | |
| P | OTC see Annex III | | | | | |
| PL | OTC see Annex III | | | | | |
| RO | Not authorised | | | | | |
| S | OTC see Annex III | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/

** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: OTC, see Annex III**

*Criteria:*
Adverse reactions related to overdose by topical application of docosanol are unlikely because of negligible per-cutaneous absorption.
Limited oral absorption makes the occurrence of adverse reactions unlikely following ingestion of docosanol.

**3.2 Paediatric use:** Not recommended for children < 12 years.

**4. COMMENTS/REFERENCES**

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Edoxudine

**1.2 ATC Code:** D06BB09 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** Treatment of muco-cutaneous herpes simplex infections.

**1.4 Posology and duration of treatment:** No data.

**1.5 Pharmaceutical forms:** -

**1.6 Contraindications:** -

**1.7 Relevant warnings:** -

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: No data from member states.

No products in PDR online, very limited information in Martindale (37th edition), and no data in *melclass* database.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** -

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Fusidic acid

**1.2 ATC Code:** D06AX01 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** Indicated either alone or in combination with systemic therapy in the treatment of primary and secondary skin infections caused by sensitive strains of *Staphylococcus aureus, Streptococcus spp* and *Corynebacterium minutissimum*.
Primary skin infections that may be expected to respond to treatment with topically-applied fusidic acid include: impetigo contagiosa, superficial folliculitis, sycosis barbae, paronychia and erythrasma.
Secondary skin infections can also be treated, such as infected eczematoid dermatitis, infected contact dermatitis and infected cuts/abrasions.

**1.4 Posology and duration of treatment:** Uncovered lesions – 3-4 times daily. Covered lesions - less frequent applications may be adequate.

**1.5 Pharmaceutical forms:** 2% ointment, 2% cream.

**1.6 Contraindications (SmPC):** Known hypersensitivity to fusidic acid/sodium fusidate or to any of the excipients.
Infection caused by non-susceptible organisms, in particular *Pseudomonas aeruginosa*.

**1.7 Relevant warnings (SmPC):** The most frequently reported adverse drug reactions are various skin reactions and, in particular, reactions at the application site.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Bacterial resistance has been reported to occur with the use of fusidic acid. As with all antibiotics, extended or recurrent use may increase the risk of developing antibiotic resistance.
Hypersensitivity reactions in the form of rashes and irritation may occur with topical fusidates.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Extended or recurrent use may increase the risk of developing contact sensitisation.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Fusidic acid is a potent antibacterial agent. Fusidic acid and its salts show fat and water solubility and strong surface activity and exhibit a particular ability to penetrate intact skin. Concentrations of 0.03 - 0.12 µg/ml fusidic acid inhibit nearly all strains of *Staphylococcus aureus.* Topical application of fusidic acid is also effective against streptococci, corynebacteria, *Neisseria* and certain clostridia.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (1) | | | | | |
| Publication** | I (1) | | | | | |
| A | Not authorised | | | | | |
| B | OTC see Annex III | | | | | |
| CH | II | | | | | |
| CZ | I | | | | | |
| E | I | | | | | |
| F | I | | | | | |
| GB | POM | | | | | |
| HR | Not authorised | | | | | |
| HU | POM | | | | | |
| I | I | | | | | |
| LV | I | | | | | |
| MK | Not authorised | | | | | |
| P | POM | | | | | |
| PL | I | | | | | |
| RO | I | | | | | |
| SLO | I | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List 1 (1)**

*Criteria:*
Self-diagnosis is not possible.
Risk of developing bacterial resistance if misused (awareness of susceptible strains is important) or if duration used is too long (extended or recurrent use).
Risk of causing contact sensitisation.

**3.2 Paediatric use:** No age limitations available.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Gentamicin

**1.2 ATC Code:** D06AX07 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** Localised skin infections (primary and secondary).
*Primary skin infections*: Impetigo contagiosa, superficial folliculitis, ecthyma, furunculosis, sycosis barbae and pyoderma gangrenosum.
*Secondary skin infections*: Infectious eczematoid dermatitis, pustular acne, pustular psoriasis, infected seborrheic dermatitis, infected contact dermatitis (including from poison ivy), infected excoriations, bacterial super-infections or fungal or viral infections.

*Martindale:* Gentamicin has also been applied topically for skin infections in concentrations of 0.1%, but such use may lead to the emergence of resistance and is considered inadvisable.

**1.4 Posology and duration of treatment:** Three or four times daily.

**1.5 Pharmaceutical forms:** 0.1% cream; 0.1% ointment.

**1.6 Contraindications (SmPC):** Gentamicin is contraindicated in patients with a known history of hypersensitivity to it, and probably in those hypersensitive to other aminoglycosides. It should be avoided in patients with myasthenia gravis, and great care is required in patients with parkinsonism and other conditions characterised by muscular weakness.

**1.7 Relevant warnings (SmPC):** Hypersensitivity reactions have occurred, especially after local use, and cross-sensitivity between aminoglycosides may occur. Very rarely, anaphylactic reactions to gentamicin have occurred.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Systemic absorption of gentamicin and other aminoglycosides has been reported after topical use on denuded skin and burns and on instillation into, and irrigation of, wounds, body-cavities (except the urinary bladder) and joints.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Use of aminoglycosides during pregnancy may damage the eighth cranial nerve of the foetus.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I | | | | | |
| Publication** | I | | | | | |
| A | I | | | | | |
| B | I | | | | | |
| BiH | I | | | | | |
| CH | I | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| CZ | Not authorised | | | | | |
| DK | Not authorised | | | | | |
| E | I | | | | | |
| F | Not authorised | | | | | |
| GB | Not authorised | | | | | |
| H | OTC see Annex III | Cutaneous | Children > 9 years | | | |
| HR | I | | | | | |
| I | I | | | | | |
| LV | Not authorised | | | | | |
| MK | I | | | | | |
| P | I | | | | | |
| PL | Not authorised | | | | | |
| RO | Not authorised | | | | | |
| SLO | I | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I**

*Criteria:*
Topical use may lead to the emergence of resistance.
Topical use may lead to systemic absorption.
Topical use may cause hypersensitivity (and cross-hypersensitivity) reactions.

**3.2 Paediatric use:** Children > 1 year. The possibility of increased absorption exists in very young children.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th and 37th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Ibacitabine

**1.2 ATC Code:** D06BB08 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** No data concerning products for cutaneous use

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | Currently not available | | | | | |
| Publication** | Currently not available | | | | | |
| A | Not authorised | | | | | |
| CZ | Not authorised | | | | | |
| F | I | | | | | |
| HR | Not authorised | | | | | |
| MK | Not authorised | | | | | |
| PL | Not authorised | | | | | |
| RO | Not authorised | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

No data concerning cutaneous use.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** -

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Idoxuridine

**1.2 ATC Code:** D06BB01 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** Idoxuridine has been used topically in the treatment of cutaneous forms of herpes simplex (and herpes zoster infections), but has generally been superseded by other antivirals.

**1.4 Posology and duration of treatment**: Idoxuridine 5% in dimethyl sulfoxide (to aid absorption) can be painted onto the lesions of cutaneous herpes simplex and herpes zoster 4 times daily for 4 days.

**1.5 Pharmaceutical forms:** Topical gel.

**1.6 Contraindications (SmPC):** Hypersensitivity.

**1.7 Relevant warnings (SmPC):** The potential teratogenicity of idoxuridine should be taken into account when treating pregnant patients or patients likely to become pregnant.
Corticosteroids should only be applied with caution in patients that are simultaneously receiving idoxuridine as they may accelerate the spread of viral infection.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Idoxuridine applied to the skin may produce irritation, stinging and hypersensitivity reactions and skin maceration. Idoxuridine is a potential carcinogen and teratogen. The occurrence of squamous carcinoma in a patient was associated with topical idoxuridine treatment.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Excessive application of topical idoxuridine to the eyes or skin may cause punctate defects in the cornea or skin maceration. Prolonged topical use should be avoided.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (1) | | | | | |
| Publication** | I (1) | | | | | |
| A | Not authorised | | | | | |
| B | Not authorised | | | | | |
| BiH | Not authorised | | | | | |
| BG | II | | | | | |
| CH | Not authorised | | | | | |
| CZ | Not authorised | | | | | |
| D | II | | | | | |
| DK | II | | | | | |
| E | II | | | | | |
| F | Not authorised | | | | | |
| GB | POM | | | | | |
| H | Not authorised | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| HR | Not authorised | | | | | |
| I | POM | | | | | |
| IRL | II + exemption Annex III | | | | | |
| LT | II | | | | | |
| MK | Not authorised | | | | | |
| NL | Not authorised | | | | | |
| P | Not authorised | | | | | |
| PL | Not authorised | | | | | |
| RO | Not authorised | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I (1)**

*Criteria:*
Possible systemic absorption after cutaneous use.

**3.2 Paediatric use:** Not recommended in children < 12 years.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th and 37th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Imiquimod

**1.2. ATC Code:** D06BB10 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** External genital and peri-anal warts (*Condylomata acuminata*) in adults; small superficial basal cell carcinomas (sBCCs) in adults; clinically-typical non-hyperkeratotic and non-hypertrophic actinic keratoses (AKs) of the face or scalp in immuno-competent adult patients when the size or number of lesions limits the efficacy and/or acceptability of cryotherapy and other topical treatment options are contraindicated or less appropriate.

**1.4 Posology and duration of treatment:** The application frequency and duration of treatment with imiquimod cream is different for each indication.
*Treatment of genital and perianal warts*: it is applied as a 5% cream 3 times each week for up to 16 weeks and is left on the skin for 6 to 10 hours.
*Management of superficial basal cell carcinoma*: a 5% cream is applied 5 times each week for 6 weeks and left on the skin for about 8 hours.
*Treatment of actinic keratoses of the face or scalp*: a 5% cream is applied twice a week for 16 weeks and is left on the skin for about 8 hours.

**1.5 Pharmaceutical forms:** 5% cream.

**1.6 Contraindications (SmPC):** Hypersensitivity.

**1.7 Relevant warnings (SmPC):** Skin reactions away from the site of application have been reported. Avoid contact with the eyes, lips and nostrils. The use of an occlusive dressing is not recommended with imiquimod cream therapy. Imiquimod has the potential to exacerbate inflammatory conditions of the skin. Application to broken skin could result in increased systemic absorption of imiquimod, leading to a greater risk of adverse events. The treated skin surface area should be protected from solar exposure. Imiquimod should be used with caution in patients with auto-immune conditions.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Adverse effects after topical application of imiquimod include local skin erosion, erythema, excoriation, flaking and oedema. There have been reports of localised hypo-pigmentation and hyper-pigmentation. Rarely, intense local inflammatory reactions including skin weeping or erosion can occur after only a few applications of imiquimod cream. Local inflammatory reactions may be accompanied or even preceded by flu-like systemic signs and symptoms including malaise, pyrexia, nausea, myalgias and rigors. Interruption of administration should be considered in such cases.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Systemic effects after topical application include headache, flu-like symptoms and myalgia. Hypotension has occurred after repeated ingestion.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (1) | | | | | |
| Publication** | I (1) | | | | | |
| A | I (1) | | | | | |
| B | I | | | | | |
| CZ | I (1) | | | | | |
| E | I | | | | | |
| F | I (1) | | | | | |
| H | Not authorised | | | | | |
| HR | I (1) | | | | | |
| MK | Not authorised | | | | | |
| PL | I | | | | | |
| RO | I (1) | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I (1)**

*Criteria:*
Self-diagnosis is not possible.
Possible systemic absorption and adverse effects.
Possible intense local inflammatory reactions.
Centrally-registered, prescription recommendation for all member states.

**3.2 Paediatric use:** Use in the paediatric patient population is not recommended. There are no data available on the use of imiquimod in children and adolescents for the approved indications. It should not be used in children with *Molluscum contagiosum* due to lack of efficacy in this indication.

## 4. COMMENTS/REFERENCES

Registered by Centralised Procedure EU/1/98/080/001-002

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).
Product Information for Aldara 5% cream (imiquimod) (Available at: http://goo.gl/OxmTd0).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Inosine
Inosine pranobex – oral form only

**1.2 ATC Code:** D06BB05 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** *Martindale:* Inosine has been used in the treatment of various viral infections including herpes simplex, genital warts and sub-acute sclerosing panencephalitis.

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: No data concerning topical skin uses are available; no data in *melclass* database.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** -

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Lysozyme

**1.2 ATC Code:** D06BB07 Chemotherapeutics for topical use, Antivirals

No data concerning topical skin products.

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | Currently not available | | | | | |
| Publication** | Currently not available | | | | | |
| A | Not authorised | | | | | |
| B | Not authorised | | | | | |
| CH | Not authorised | | | | | |
| CZ | Not authorised | | | | | |
| D | OTC see Annex III | Cutaneous | | | | |
| F | Not authorised | | | | | |
| HR | Not authorised | | | | | |
| I | Not authorised as mono-product | | | | | |
| P | Not authorised | | | | | |
| PL | Not authorised | | | | | |
| RO | Not authorised | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

No data concerning cutaneous uses.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** -

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Mafenide

**1.2 ATC Code:** D06BA03 Chemotherapeutics for topical use, Sulfonamides

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | Currently not available | | | | | |
| Publication** | Currently not available | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from member states.

Not authorised in member states.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** Use of mafenide is not recommended in premature or new-born infants up to 2 months of age. Sulfonamide medicines may cause liver problems in such infants.

## 4. COMMENTS/REFERENCES

It is marketed mainly in the USA. It is not authorised d in member states.

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Metronidazole

**1.2 ATC Code:** D06BX01 Chemotherapeutics for topical use, Other chemotherapeutics

**1.3 Therapeutic indications:** Treatment of exacerbations of rosacea.

**1.4 Posology and duration of treatment:** The average period of treatment is three to four months. The recommended duration of treatment should not be exceeded. In the absence of a clear clinical improvement, therapy should be stopped. Adults: twice daily, morning and evening.

**1.5 Pharmaceutical forms:** 0.075% cream; 1% cream; 1% gel; 10% ointment.

**1.6 Contraindications (SmPC):** Hypersensitivity.

**1.7 Relevant warnings (SmPC):** Contact with the eyes should be avoided. Metronidazole is a nitroimidazole and should be used with care in patients with evidence or a history of blood dyscrasia. Exposure of treated sites to ultraviolet (e.g. solarium, sun-lamp) or strong sunlight (including sun-bathing) should be avoided while using metronidazole. Unnecessary and prolonged use of this medication should be avoided.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** *Skin and subcutaneous tissue disorders*: dry skin, erythema, pruritus, skin discomfort (burning, skin pain, stinging), skin irritation, worsening of rosacea, contact dermatitis.
*Nervous system disorders* (uncommon): hypothesia, paraesthesia, dysgeusia (metallic taste).
*Gastrointestinal disorders* (uncommon): nausea.
Watery eyes have been reported if applied too closely to this area.

**2.1.1 Recent cases at European level:**

**2.1.2. Indirect risks (incorrect use):** Interaction with systemic medication is unlikely because absorption of metronidazole following cutaneous application is low.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I | | | | | |
| Publication** | I | | | | | |
| B | I | | | | | |
| CZ | I (1) | | | | | |
| E | I | | | | | |
| F | I | | | | | |
| HR | II | | | | | |
| I | II | | | | | |
| LV | I (1) | | | | | |
| MK | I | | | | | |
| PL | I | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| RO | Not authorised | | | | | |
| SLO | I | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I**

*Criteria:*
Risk of systemic absorption.
Long-term treatment.
Possibility of inappropriate use.

**3.2 Paediatric use:** Safety and effectiveness in paediatric patients have not been established.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Mupirocin

**1.2 ATC Code:** D06AX09 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** Treatment of various bacterial skin infections.

**1.4 Posology and duration of treatment:** 2 to 3 times daily for up to 10 days; treatment should be re-evaluated if there is no response after 3 to 5 days.

**1.5 Pharmaceutical forms:** 2% ointment in a macrogol base; 2% cream containing mupirocin calcium.

**1.6 Contraindications (SmPC):** for ophthalmic or nasal use.

**1.7 Relevant warnings (SmPC):** Mupirocin is usually well tolerated, but local reactions such as burning, stinging and itching may occur after the application of mupirocin to the skin. As with other antibacterial products, prolonged use may result in proliferation of non-susceptible organisms, including fungi.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Local reactions such as burning, stinging and itching may occur after the application of mupirocin to the skin. Penetration of mupirocin into the deeper epidermal and dermal layers of the skin is enhanced in traumatised skin and under occlusive dressings.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Some mupirocin products are formulated in a macrogol base: such formulations are not suitable for application to mucous membranes and should be used with caution in patients with extensive burns or wounds because of the possibility of macrogol toxicity. Care is also required in patients with renal impairment.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Mupirocin is an antibacterial agent that inhibits bacterial protein synthesis by binding to isoleucyl transfer RNA synthetase. It is primarily bacteriostatic at low concentrations, although it is usually bactericidal in the high concentrations achieved by topical application to the skin. At these concentrations it may have some activity against organisms reported to be relatively resistant to mupirocin *in vitro*.
Only very small amounts of topically-applied mupirocin are absorbed into the systemic circulation, where it is rapidly metabolised to monic acid.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I | | | | | |
| Publication** | I | | | | | |
| A | Not authorised | | | | | |
| B | I | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| BG | II | | | | | |
| CH | II | | | | | |
| CZ | I | | | | | |
| D | II | | | | | |
| DK | I | | | | | |
| E | II | | | | | |
| F | I | | | | | |
| FIN | II | | | | | |
| GB | POM | | | | | |
| H | II | | | | | |
| HR | I | | | | | |
| I | II | | | | | |
| IRL | II | | | | | |
| LV | I | | | | | |
| MK | I | | | | | |
| NL | POM | | | | | |
| P | II | | | | | |
| PL | I | | | | | |
| RO | Not authorised | | | | | |
| S | II | | | | | |
| SLO | II | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I**

*Criteria:*
Prolonged use may lead to proliferation of resistant bacteria/fungi.
Possible systemic absorption after topical use.
Possible hypersensitivity reactions.

**3.2 Paediatric use**: Children > 1 year.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th and 37th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Neomycin

**1.2 ATC Code:** D06AX04 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** Neomycin sulfate salt is a broad-spectrum bactericidal antibiotic that is effective against the majority of bacteria commonly associated with skin infections.
*OTC:* First aid to help prevent infection in minor cuts, scrapes and burns.

**1.4 Posology and duration of treatment:** External use only; 1-3 times daily on clean skin.

**1.5 Pharmaceutical forms:** 0.35% and 0.5% ointment; 1.7% spray.

**1.6 Contraindications (SmPC):** Due to the known ototoxic and nephrotoxic potential of neomycin, its use in large quantities or on large areas for prolonged periods of time is not recommended in circumstances where significant systemic absorption may occur.
*OTC:* Do not use in the eyes, over large areas of the body, if allergic to any of the ingredients or for longer than one week unless directed by a doctor.

**1.7 Relevant warnings (SmPC):** Hypersensitivity reactions (such as rashes, pruritus and, sometimes, drug fever or even anaphylaxis) frequently occur during localised treatment with neomycin. Cross-sensitivity with other aminoglycosides may occur.
Interactions: Absorption after oral or localised use may be sufficient to produce interactions with other drugs given systemically.
There is little information to demonstrate a possible effect of topically-applied neomycin during pregnancy and lactation. However, neomycin present in maternal blood can cross the placenta and may give rise to a theoretical risk of foetal toxicity, so it is not recommended for use during pregnancy or lactation.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Neomycin has particularly potent nephrotoxic and ototoxic properties and so is generally no longer given parenterally. However, sufficient amounts may be absorbed after use by other dosage routes (e.g. instillation into open wounds or topical application to damaged skin) to produce irreversible partial or total deafness. The effect is dose-related and is enhanced by renal impairment. Nephrotoxic effects may also occur.

**2.1.1 Recent cases at European level:** -

**2.1.2. Indirect risks (incorrect use):** The topical use of neomycin in patients with extensive skin damage or perforated tympanic membranes may result in deafness. Prolonged local use should be avoided as it may lead to skin sensitisation and possible cross-sensitivity to other aminoglycosides.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Neomycin is an aminoglycoside antibiotic used topically in the treatment of infections of the skin, ear and eye due to susceptible staphylococci and other organisms. Most preparations contain the sulfate, but neomycin undecenoate is also used. Neomycin has a mode of action and spectrum of activity similar to that of gentamicin, but it lacks activity against

*Pseudomonas aeruginosa*. It is reported to be active against *Mycobacterium tuberculosis*. Because of its extensive topical use, resistance has been reported to be relatively widespread; notably among staphylococci and some *Salmonella*, *Shigella* and *Escherichia coli* strains. Cross-resistance with kanamycin, framycetin and paromomycin occurs.
The topical use of neomycin in patients with extensive skin damage or perforated tympanic membranes may result in deafness.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I + Exemption Annex III | Cutaneous | For adults and children > 12 years; short-term use (no longer than 7 days); not for large surfaces; combination products with other antibiotics only (e.g. bacitracin) | | | |
| Publication** | I + Exemption Annex III | Cutaneous | For adults and children > 12 years; short-term use (no longer than 7 days); not for large surfaces; combination products with other antibiotics only (e.g. bacitracin) | | | |
| A | Not authorised - Combination products only (List I) | | | | | |
| B | Not authorised - Combination products only | | | | | |
| BiH | Not authorised | | | | | |
| CH | Not authorised | | | | | |
| E | I | | | | | |
| F | Not authorised - Combination products only | | | | | |
| GB | Not authorised | | | | | |
| H | Not authorised | | | | | |
| HR | Not authorised - Combination products only (List I) | | | | | |
| I | Not authorised - Combination products only (OTC) | | | | | |
| MK | Not authorised - Combination products only (List I) | | | | | |
| P | Not authorised - Combination products only | | | | | |
| PL | I + Exemption Annex III | Cutaneous | Ointment | 0.5% | | 5 g |
| RO | Not authorised - Combination products only (with bacitracin) (OTC) | | | | | |
| SLO | I | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I + Exemption Annex III**
*Exemptions:*

- Combination products with other antibiotics only;
- For cutaneous use;
- No longer than 7 days;
- Adults and children > 12 years;
- Not for use on large surfaces.

**3.2 Paediatric use:** A possibility of increased absorption exists in very young children, so neomycin is not recommended for use in neonates and infants (up to 2 years). In neonates and infants, absorption by immature skin may be enhanced, and renal function may not be fully developed.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Oxytetracycline

**1.2 ATC Code**: D06AA03 Antibiotics for topical use, Tetracycline and derivatives

**1.3 Therapeutic indications**: Skin infections; mild inflammatory acne and as an adjunct to systemic treatment in more severe forms of rosacea (long-term treatment).
It may be used alone or with one or more other medicines that are applied to the skin, or taken systemically for acne.

**1.4 Posology and duration of treatment:** -

**1.5 Pharmaceutical forms:** Always together with other agents.
Oxytetracycline and its salts have been applied topically, often with other agents, as a variety of eye and ear drops, ointments, creams and sprays.
Topical powder: oxytetracycline hydrochloride and polymyxin B sulfate.
Ointment 3%: oxytetracycline hydrochloride and hydrocortisone, oxycort and polymyxin B sulfate.

**1.6 Contraindications (SmPC):** Hypersensitivity.

**1.7 Relevant warnings (SmPC):** Side effects: pain, redness, swelling or other sign of irritation not present before use of this medicine.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** It causes photosensitivity, possible super-infections of *Saccharomyces* or other resistant strains and scalded skin syndrome (rarely). Oxytetracycline may produce less tooth discolouration than some other tetracyclines, but gastrointestinal symptoms tend to be more severe.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Oxytetracycline is a tetracycline derivative with actions and uses similar to those of tetracycline. Anti-microbial action is as for tetracycline, but it is somewhat less active against many of the same target organisms.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (combination products) | | | | | |
| Publication** | I (combination products) | | | | | |
| A | Veterinary use only | | | | | |
| B | Not authorised as mono-product - Only in combination with polymyxin | | | | | |
| E | I | | | | | |
| F | Not authorised | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| H | OTC | | No OTC details | | | |
| HR | Not authorised | | | | | |
| MK | Not authorised as mono-product - Combination products with other antibiotics only | | | | | |
| PL | Not authorised as mono-product - Combination products with other antibiotics only | | | | | |
| RO | Not authorised as mono-product - Combination products with other antibiotics only | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

For topical use - available as combination products only.

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

**Recommendation: Not to classify as mono-product**

Combined preparations, which contain oxytetracycline and other antibiotics, are classified in D06AA03 – oxytetracycline.

**Recommendation for combination product: List I**

*Criteria:*
Risk of sensitisation and it may contribute to the development of resistance.
Possibility of super-infections of *Saccharomyces* or other resistant strains.
Possible hypersensitivity and cross-hypersensitivity reactions.

**3.2 Paediatric use:** Children > 12 years, as for other tetracyclines.

## 4. COMMENTS/REFERENCES

Topical skin products containing oxytetracycline as a single active substance are not available.

**References:**
Martindale: The Complete Drug Reference, 35th and 37th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Penciclovir

**1.2 ATC Code:** D06BB06 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** Adults and children > 12 years: treatment of herpes labialis.

**1.4 Posology and duration of treatment:** Every 2 hours during waking hours for 4 days; treatment should be started as early as possible (i.e. during the prodrome or when lesions [blisters] appear).

**1.5 Pharmaceutical forms:** 1% cream.

**1.6 Contraindications (SmPC):** Hypersensitivity to penciclovir and famciclovir.

**1.7 Relevant warnings (SmPC):** Application to human mucous membranes is not recommended. Particular care should be taken to avoid application in or near the eyes since it may cause irritation. Lesions that do not improve or that worsen on therapy should be evaluated for secondary bacterial infection.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Isolated cases of hypersensitivity reactions, such as allergic dermatitis, rash, urticaria, pruritis and oedema.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Since penciclovir is poorly absorbed following oral administration, adverse reactions related to penciclovir ingestion are unlikely.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I + Exemption Annex III | Cutaneous | Adults and children > 12 years; for short-term treatment (no longer than 10 days); for early symptoms of herpes labialis | 1% | | 20mg |
| Publication** | I + Exemption Annex III | Cutaneous | Adults and children > 12 years; for short-term treatment (no longer than 10 days); for early symptoms of herpes labialis | 1% | | 20mg |
| A | I (1) + exemption Annex III | | | | | |
| B | OTC see Annex III | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| BG | II | | | | | |
| CH | II + Exemption Annex III | | | | | |
| CZ | OTC see Annex III | | | | | |
| D | II + Exemption Annex III | | | | | |
| DK | II + Exemption Annex III | | | | | |
| E | II | | | | | |
| F | I + Exemption Annex III | | | | | |
| FIN | I + Exemption Annex III | | | | | |
| GB | II + Exemption Annex III | | | | | |
| H | OTC see Annex III | | | | | |
| HR | Not authorised | | | | | |
| I | OTC see Annex III | | | | | |
| IRL | II | | | | | |
| LT | OTC see Annex III | | | | | |
| LV | OTC see Annex III | | | | | |
| MK | Not authorised | | | | | |
| NL | OTC see Annex III | | | | | |
| P | II | | | | | |
| PL | Not authorised | | | | | |
| RO | Not authorised | | | | | |
| S | II + Exemption Annex III | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I + Exemption Annex III**
*Exemptions:*

- Cutaneous use;
- For adults and children > 12 years;
- Short-term treatment of early symptoms of herpes labialis;
- MS: 1%; MQP: 20mg.

**3.2 Paediatric use:** Children > 12 years.

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Podophyllotoxin
*BP 2005 (Podophyllum Resin)*: The resin obtained from the rhizomes and roots of *Podophyllum hexandrum* (*P. emodi*). It contains not less than 50% of total aryltetralin lignans, calculated as podophyllotoxin.

**1.2 ATC Code:** D06BB04 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** *Podophyllum* preparations are one of the treatment choices for ano-genital warts caused by human papillomavirus infection (*Condylomata acuminata*).

**1.4 Posology and duration of treatment:** Preparations containing podophyllotoxin 0.5% in alcohol (or an alcoholic gel) or a 0.15% podophyllotoxin cream are used similarly. These preparations are applied twice daily for 3 days, but not washed off. Treatment may be repeated at weekly intervals for up to a total of 5 weeks of treatment.

**1.5 Pharmaceutical forms:** 0.5% alcohol solution, alcoholic gel; 0.15% cream.

**1.6 Contraindications (SmPC):** Hypersensitivity; *Podophyllum* resin should not be used on cervical or urethral warts.

**1.7 Relevant warnings (SmPC):** Only a small area or number of warts should be treated at any one time. Care must be taken to avoid application to healthy tissue. *Podophyllum* resin is also used with other keratolytics for the removal of plantar warts.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** *Podophyllum* is a very strong irritant, especially when applied to the eyes and mucous membranes. It can also cause severe systemic toxicity after ingestion or topical application, which is usually reversible, but has been fatal. Symptoms of toxicity include nausea, vomiting, abdominal pain and diarrhoea; though there may also be indications of thrombocytopaenia, leucopaenia, renal failure and hepatotoxicity. Onset of CNS effects are delayed, but prolonged in duration and include acute psychotic reactions, hallucinations, confusion, dizziness, stupor, ataxia, hypotonia, seizures and coma. Electorencephalogram (EEG) signatures may persist for several days.
Peripheral and autonomic neuropathies develop later and may result in paraesthesias, reduced reflexes, muscle weakness, tachycardia, apnoea, orthostatic hypotension, paralytic ileus and urinary retention. Neuropathy may improve, but full recovery is unusual.
There is a report of the transformation of a condyloma acuminatum into an invasive squamous cell carcinoma after treatment with podophyllum 25% in alcohol.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** There have been a few cases of incorrect use arising from consumption of herbal preparations containing *Podophyllum* or the related plant bajiaolian (*Dysosma pleianthum*). Death has occurred after ingestion of 10 g of *Podophyllum* resin.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I | | | | | |
| Publication** | I | | | | | |
| A | I (1) | | | | | |
| B | Not authorised | | | | | |
| CH | I | | | | | |
| CZ | I | | | | | |
| D | II | | | | | |
| E | I | | | | | |
| F | I | | | | | |
| GB | POM | | | | | |
| HR | Not authorised | | | | | |
| I | II | | | | | |
| LV | I (1) | | | | | |
| MK | Not authorised | | | | | |
| NL | II | | | | | |
| P | II | | | | | |
| PL | I | | | | | |
| RO | I (1) | | | | | |
| SLO | I | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I**

*Criteria:*
Self-diagnosis is not possible.
It has a very strong irritant effect, especially when applied to the eyes and mucous membranes.
It can cause severe systemic toxicity after ingestion or topical application, which is usually reversible, but has been fatal.

**3.2 Paediatric use:** Safety and effectiveness in paediatric patients have not been established.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Racecadotril

**1.2 ATC Code:** A07XA04 Antidiarrheals, intestinal, antiinflammatory/Antiinfective agents, Other antidiarrheals

**1.3 Therapeutic indications:** Treatment of acute diarrhoea; chronic diarrhoea related to HIV infection or AIDS.

**1.4 Posology and duration of treatment:** Oral.
*Adult*: Treatment of acute diarrhoea: 100 mg 3 times daily, not longer than 7 days.
*Paediatric*: For children older than 3 months: 1.5 mg/kg 3 times daily, not longer than 5 days.

**1.5 Pharmaceutical forms:** Capsules and oral solution.

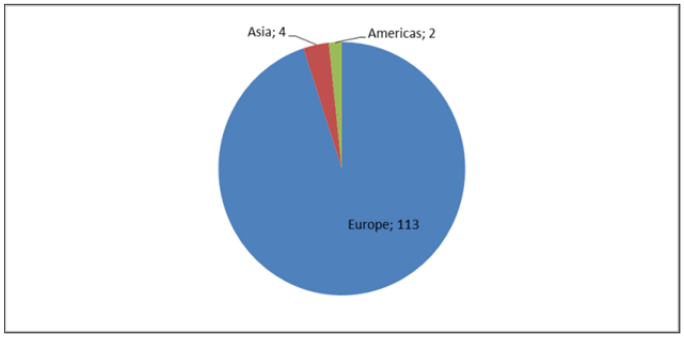
**1.6 Contraindications (SmPC):**
*Contraindications:* Prior hypersensitivity to racecadotril or ecadotril (sinorphan).
*Precaution:* intestinal function disorders (potential exacerbation); dysenteric syndrome with bloody stools/fever; presence of dehydration.

**1.7 Relevant warnings (SmPC): -**

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):**
Persistence of hypokalaemia has been infrequently reported in children with severe watery diarrhoea on treatment with racecadotril; although, this was more likely related to the acute diarrhoea. Constipation during treatment has also been infrequently reported, once placebo effects are eliminated, and is less frequent than reported with the use of loperamide. In one trial in adults (n=157), rebound constipation (not passing a stool for at least 2 days during treatment) occurred in 19% and 10% of patients receiving loperamide and racecadotril, respectively. Another study showed that the overall gastro-intestinal tolerability of racecadotril was better than that of loperamide; constipation after resolution of diarrhoea was seen in 8% and 31% of patients, respectively.
Available studies show that abdominal distension does not occur more commonly with use of racecadotril compared to placebos. Ileus has occurred rarely, though this was more likely related to the underlying condition.
Vomiting has been reported to occur in up to 50% of children treated with racecadotril, although a high incidence has also been seen with use of a placebo. Correcting for placebo effects, the incidence of vomiting in children is low (less than 10%).
Dizziness, malaise and headache have accompanied racecadotril therapy of acute diarrhoea in a few patients; although a causal link is doubtful.

WHO data (up to March 2011 – 119 reports):



The most frequently reported ADRs are of skin and gastrointestinal disorders. Among the top 20 most reported ADRs are urticaria, rash and pruritus (each with about 10 reports). Other ADRs have fewer than 8 reports each (e.g. allergic reactions).

*Interactions:* Not known.

*Common adverse reactions:*
*Gastrointestinal*: vomiting, abdominal distension.
*Neurologic*: headache, dizziness, malaise.
*Skin*: erythema, rash.
*Other*: hypokalemia.

Racecadotril appears to be an equally effective and less toxic alternative to anti-motility agents (e.g. loperamide, diphenoxylate) in the management of acute diarrhoea. The lack of anti-transit effects with racecadotril may diminish the potential for bacterial colonisation, abdominal distension and toxic megacolon, which are concerns with anti-motility agents. Consequent constipation may also occur less frequently with racecadotril therapy. Racecadotril should be considered a first-line or second-line therapy for acute diarrhoea, particularly in children and the elderly.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription Status | Exemption | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (3) + Exemption Annex III | Oral | Adults only; short-term treatment (max 3 days); max 300mg/day | | | |
| Publication** | I (3) + Exemption Annex III | Oral | Adults only; short-term treatment (max 3 days); max 300mg/day | | | |
| A | I | | | | | |
| B | I + Exemption Annex III | Oral | Only adults (OTC) | 100mg | | |
| D | I (1) + Exemption Annex III | Oral | | | | |
| E | I | Oral | | | | |
| F | II + Exemption Annex III | | | | | |
| HR | I | | | | | |
| I | II | | | | | |
| MK | I | | | | | |
| PL | I + Exemption Annex III | Oral | Treatment of acute diarrhoea in adults; no longer than 7 days | 100mg | 300mg | |
| RO | I | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I (3) + Exemption Annex III**

*Exemptions:*

- Oral use;
- Adults only;
- Short-term therapy (maximum 3 days) for acute diarrhoea;
- Maximum 300 mg/day.

As effective as loperamide, but it seems to be less toxic.

**3.2. Paediatric use:** Oral use not recommended for children under 3 months. Short-term therapy, i.e. 3 days maximum.

## 4. COMMENTS/REFERENCES

### 4. References:

Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
HALMED - Agency for Medicinal Products and Medical Devices of Croatia (Available at: http://goo.gl/Fi0mEp) (Hydrasec).
WHO Drug Dictionary Browser (Available at: https://vigisearch.who-umc.org/dd_browser).
VigiSearch (Available at: https://vigisearch.who-umc.org/vigisearch).
*Melclass* database (Available at: http://www.edqm.eu/melclass/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Retapamulin

**1.2 ATC Code:** D06AX13 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** Short-term treatment of superficial skin infections such as impetigo, infected small lacerations, abrasions or sutured wounds.

**1.4 Posology and duration of treatment:** Topically twice daily for 5 days (infants > 9 months only and apply to no more than 2% of body surface area in patients younger than 18 years). Alternative therapy should be considered if there is no improvement or a worsening in the infected area after 2-3 days of treatment.

**1.5 Pharmaceutical forms**: 1% ointment.

**1.6 Contraindications (SmPC):** Known or suspected hypersensitivity.

**1.7 Relevant warnings (SmPC):** Prolonged use may result in proliferation of non-susceptible micro-organisms, including fungi. It may cause sensitisation or severe local irritation. Retapamulin should not be used to treat abscesses. Retapamulin should not be used to treat infections known or thought likely to be due to MRSA (Methicillin-resistant *Staphylococcus aureus*).

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Hypersensitivity including angioedema, contact dermatitis, application site reactions (irritation, pain, pruritus, erythema, burning). Prolonged use of retapamulin may result in proliferation of non-susceptible micro-organisms, including fungi.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Retapamulin ointment must be kept away from the eyes and mucous membranes. Epistaxis has been reported with the use of retapamulin on nasal mucosa. Care must be taken to avoid ingestion.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Retapamulin is a semi-synthetic derivative of the compound pleuromutilin, which is isolated through fermentation from *Clitopilus passeckerianus* (formerly *Pleurotus passeckerianus*). Retapamulin selectively inhibits bacterial protein synthesis by interacting with a unique site on the 50S sub-unit of the bacterial ribosome, which is distinct from the binding sites of other non-pleuromutilin antibacterial agents that interact with the ribosome. Retapamulin is predominantly bacteriostatic against *S. aureus* and S*. pyogenes*. Due to its distinct mode of action, target-specific cross-resistance with other classes of antibacterial agents is rare. Systemic exposure following topical application of retapamulin through intact skin has been reported as being very low.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (1) | | | | | |
| Publication** | I (1) | | | | | |
| A | I (1) | | | | | |
| B | POM | | | | | |
| CZ | I | | | | | |
| D | I | | | | | |
| F | I | | | | | |
| I | II | | | | | |
| MK | Not authorised | | | | | |
| PL | I | | | | | |
| RO | I (1) | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I (1)**

*Criteria:*
Prolonged use of retapamulin may result in proliferation of non-susceptible micro-organisms, including fungi.
It may cause hypersensitivity including angioedema, contact dermatitis and application site reactions.
It is a relatively new, centrally-registered product and the recommended classification for all member states is List I.

**3.2 Paediatric use:** The safety and efficacy of retapamulin ointment in infants less than 9 months of age has not been established. Thus, retapamulin is not recommended for use in children aged less than 9 months.

## 4. COMMENTS/REFERENCES

Registered by the Centralised Procedure EU/1/07/390/001-004.

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
European Medicines Agency (Available at: http://www.ema.europa.eu/ema/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Rifaximin

**1.2 ATC Code:** D06AX11 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** Rifaximin is a rifamycin anti-bacterial agent with anti-microbial actions similar to those of rifampicin. However, it is poorly absorbed from the gastrointestinal tract. It has been administered orally in the treatment of gastrointestinal infections (including travellers' diarrhoea), as a prophylactic for surgical infection, and to reduce hyperammonaemia in hepatic encephalopathy. Doses have ranged from 10-15 mg/kg/day or from 600-1200 mg/day, in either case in divided doses. Rifaximin has also been used topically as a 5% ointment.

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | Currently not available | | | | | |
| Publication** | Currently not available | | | | | |
| PL | Not authorised | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

There is very limited data for topical skin use in the Martindale reference.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** -

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Sinecatechins

*PDR information:* sinecatechins are a mixture of catechins and other green tea components such as *Epigallocatechin gallate* (EGCg), other catechin derivatives such as *Epicatechin* (EC), *Epigallocatechin* (EGC), *Epicatechin gallate* (ECg), and some additional minor catechin derivatives, i.e. *Gallocatechin gallate* (GCg), *Gallocatechin* (GC), *Catechin gallate* (Cg), and *Catechin* (C).

**1.2 ATC Code:** D06BB12 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** Topical treatment of external genital and peri-anal warts (*Condylomata acuminata*) in immuno-competent patients aged 18 years and older.

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

No data in *Melclass* database.
No data available from member states.
It is marketed mainly in the USA. It is not authorised in member states.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** Safety and effectiveness in paediatric patients have not been established.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.

Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Silver sulfadiazine

**1.2 ATC Code:** D06BA01 Chemoterapeutics for topical use, Sulfonamides

**1.3 Therapeutic indications:** Prevention and treatment of infection in severe burns; other skin conditions (such as leg ulcers) where infection may prevent healing and for the prophylaxis of infection in skin grafting.

**1.4 Posology and duration of treatment:** 1-2 times daily directly on the burned skin. A 1-2 mm layer of cream should stay on the skin until the wound is completely healed.

**1.5 Pharmaceutical forms:** 1% cream.

**1.6 Contraindications (SmPC):** Hypersensitivity to silver sulfadiazine and/or to silver.

**1.7 Relevant warnings (SmPC):** Sulfadiazine silver slowly releases sulfadiazine when in contact with wound exudates. Up to about 10% of the sulfadiazine may be absorbed; concentrations in blood of 10- 20 µg/ml have been reported, although higher concentrations may be achieved when extensive areas of the body are treated. Some silver may also be absorbed.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** Local pain or irritation is uncommon. Separation of the eschar may be delayed and fungal invasion of the wound may occur.
One study reported that silver sulfadiazine delays healing of wounds.
*PDR*: Because sulfonamide therapy is known to increase the possibility of kernicterus, sulfadiazine silver cream 1% should not be used on pregnant women approaching full- or at term, on premature infants, or on new-born infants during the first 2 months of life.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Absorption of silver sulfadiazine varies depending on the percentage of body surface area it is administered to and the extent of the tissue damage. Although few ADRs have been reported, it is possible that any adverse reaction typically associated with sulfonamides may occur.
Some of the adverse reactions that have been associated with sulfonamides are: blood dyscrasias (including agranulocytosis, aplastic anaemia, thrombocytopaenia, leucopenia and hemolytic anaemia); dermatologic and allergic reactions (including Stevens-Johnson syndrome and exfoliative dermatitis); gastrointestinal reactions; hepatitis and hepatocellular necrosis; CNS reactions; and toxic nephrosis. Transient leucopenia does not usually require cessation of the use of sulfadiazine silver, but blood counts should be monitored to ensure they return to normal within a few days. Systemic absorption of silver, resulting in argyria, can occur when sulfadiazine silver is applied to wounds covering large areas or over prolonged periods. There is a report of argyria, with discolouration of the skin and sensorimotor neuropathy, caused by excessive application of sulfadiazine silver 1% cream to extensive leg ulcers.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Sulfadiazine silver has broad anti-microbial activity against Gram-positive and Gram-negative bacteria, including *Pseudomonas aeruginosa*, and some yeasts and fungi. Sulfadiazine silver has a bactericidal action; in contrast to sulfadiazine, the silver salt acts primarily on the cell

membrane and cell wall and its action is not antagonised by *p*-aminobenzoic acid. Resistance to sulfadiazine silver has been reported and may develop during therapy.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I + Exemption Annex III | Cutaneous | Adults only; small surfaces; < 7 days | 1% | | 50mg |
| Publication** | I +Exemption Annex III | Cutaneous | Adults only; small surfaces; < 7 days | 1% | | 50mg |
| A | Not authorised | | | | | |
| B | OTC see Annex III | | | | | |
| BG | OTC see Annex III | | | | | |
| BiH | POM | | | | | |
| CH | II + Exemption Annex III | | | | | |
| CZ | Not authorised | | | | | |
| D | II | | | | | |
| DK | II | | | | | |
| E | II | | | | | |
| F | I | | | | | |
| FIN | II | | | | | |
| GB | I | | | | | |
| H | OTC see Annex III | | | | | |
| HR | I | | | | | |
| I | POM | | | | | |
| IRL | II | | | | | |
| LV | II | | | | | |
| MK | I | | | | | |
| N | II | | | | | |
| NL | II | | | | | |
| P | I | | | | | |
| PL | Not authorised | | | | | |
| RO | OTC see Annex III | | | | | |
| SLO | II | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List 1 + Exemption Annex III**
*Exemptions:*

- Cutaneous use;
- For minor burns (small surfaces only);
- Treatment for no longer than 7 days;
- Adults only;
- MS: 1%, MQP: 50mg.

**3.2 Paediatric use:** No data.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th and 37th edition.

Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Sulfamerazine

**1.2 ATC Code:** D06BA06 Chemotherapeutics for topics use, Sulfonamides

**1.3 Therapeutic indications:** Sulfamerazine is a short-acting sulfonamide with properties similar to those of sulfamethoxazole. It is usually administered with other sulfonamides or with trimethoprim.

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

No data concerning cutaneous use are available.

Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: No data (deleted from the *melclass* database).

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** -

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Sulfamethizole

**1.2 ATC Code:** D06BA04 Chemotherapeutics for topical use, Sulfonamides

**1.3 Therapeutic indications:** Sulfamethizole is a short-acting sulfonamide that is administered orally for the treatment of urinary tract infections, sometimes with other anti-bacterial agents. It is unsuitable for the treatment of systemic infection since only relatively low concentrations of drug are absorbed into the blood and tissues.

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions:
No data in *melclass* database.
No data concerning cutaneous use are available.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** -

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Sulfanilamide

**1.2 ATC Code:** D06BA05 Chemotherapeutics for topical use, Sulfonamides

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Sulfanilamide is a short-acting sulfonamide with properties similar to those of sulfamethoxazole. Its anti-bacterial activity is less than that of sulfamethoxazole. It has been used topically (including vaginally) for the treatment of susceptible infections, often with other drugs.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | Currently not available | | | | | |
| Publication** | Currently not available | | | | | |
| A | Not authorised | | | | | |
| B | Not authorised | | | | | |
| CZ | Not authorised | | | | | |
| F | Not authorised | | | | | |
| HR | Not authorised | | | | | |
| LV | OTC see Annex III | | | | | |
| MK | Not authorised | | | | | |
| PL | Not authorised | | | | | |
| RO | Not authorised | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/

** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

No data concerning cutaneous use are available.

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

**Recommendation: Not to classify**

**3.2 Paediatric use:** -

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Sulfathiazole

**1.2 ATC Code:** D06BA02 Chemotherapeutics for topical use, Sulfonamides

**1.3 Therapeutic indications:** Burns (also radiation burns); persistent leg ulcers; bedsores.

**1.4 Posology and duration of treatment:** layer of 1-2 mm twice daily.

**1.5 Pharmaceutical forms:** 2% cream.

**1.6 Contraindications (SmPC):** Hypersensitivity; not recommended in neonates < 2 months, during pregnancy and lactation; congenital glucose-6-phosphate dehydrogenase deficiency.

**1.7 Relevant warnings (SmPC):** During long-term (topical) use over large surface areas, it can cause damage to the kidneys, liver or bone marrow, as well as aplastic anaemia and/or haemolytic anaemia.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** -

**2.1.1 Recent cases at European level:** Hypersensitivity reactions in the form of rashes, irritation and itching may occur.

**2.1.2 Indirect risks (incorrect use):** During long-term (topical) use over large surface areas, it can cause damage to the kidneys, liver or bone marrow, as well as aplastic anaemia and/or haemolytic anaemia.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Sulfathiazole is a short-acting sulfonamide with properties similar to those of sulfamethoxazole. It used to be a common oral and topical anti-microbial treatment option until less toxic alternatives were discovered. It is still occasionally used (sometimes in combination with sulfabenzamide and sulfacetamide) in preparations for the topical treatment of vaginal infections, and with other drugs in the treatment of skin infections. It is now rarely used systemically due to its toxicity.

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I | | | | | |
| Publication** | I | | | | | |
| A | Not authorised | | | | | |
| B | Not authorised | | | | | |
| BiH | Not authorised | | | | | |
| CZ | Not authorised | | | | | |
| DK | Not authorised | | | | | |
| E | I | | | | | |
| F | Not authorised | | | | | |
| GB | Not authorised | | | | | |
| H | Not authorised | | | | | |
| HR | Not authorised | | | | | |
| I | Not authorised | | | | | |
| LV | II | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| MK | Not authorised | | | | | |
| PL | I | | | | | |
| RO | Not authorised | | | | | |
| S | Not authorised | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I**

*Criteria:*
Risk of severe systemic adverse reactions.

**3.2 Paediatric use:** Not recommended in infants < 2 months old.

## 4. COMMENTS/REFERENCES

**References:**
Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Tetracycline

**1.2 ATC Code:** D06AA04 Antibiotics for topical use, Tetracycline and derivatives

**1.3 Therapeutic indications:** Skin infections; mild inflammatory acne and as an adjunct to systemic treatment in more severe forms of rosacea (long-term treatment).
It may be used alone or with one or more other medicines that are applied to the skin or taken systemically for acne.

**1.4 Posology and duration of treatment:** The dose is different for different patients. The number of doses, the time between doses and the duration of treatment depends on the medical problem (usually 4-6 weeks and no longer than 12 weeks).
*OTC dosage according to PDR:*
For skin infections: Adults and children - one or two times a day.
For acne: Adults and children over 11 years of age - two times a day.

**1.5 Pharmaceutical forms:** Tetracycline hydrochloride for topical solution (2%); Tetracycline hydrochloride ointment 3%.

**1.6 Contraindications (SmPC):** Hypersensitivity for any drug of this group; children < 12 years (OTC); pregnancy; lactation.

**1.7 Relevant warnings (SmPC):** Because of possible antagonism to the action of penicillins by the predominantly bacteriostatic tetracyclines, it has been recommended that the two types of drug should not be used together.
*OTC warning (according to PDR):* it should not be used further without a doctor's recommendation if there are no signs of improvement or the condition worsens (following 2 weeks of treatment).

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** It causes photo-sensitivity, possible *Saccharomyces* or resistant strain super-infections or, rarely, scalded skin syndrome.
Side effects: Pain, redness, swelling or other signs of irritation not present before use of this medicine.

**2.1.1 Recent cases at European level: -**

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I (1) | | | | | |
| Publication** | I (1) | | | | | |
| A | Not authorised | | | | | |
| B | Not authorised | | | | | |
| BiH | Not authorised | | | | | |
| CZ | Not authorised | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| E | Not authorised | | | | | |
| F | Not authorised | | | | | |
| HR | Not authorised as mono-product | | | | | |
| LV | I (1) | | | | | |
| MK | Not authorised | | | | | |
| P | Not authorised | | | | | |
| PL | I | | | | | |
| RO | I | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

Topical ointment forms of tetracyclines are available without a prescription in the USA (PDR).

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

**Recommendation: List 1 (1)**

*Criteria:*
Long-term use.
Possible *Saccharomyces* or resistant strain super-infections.
Possible hypersensitivity and cross-hypersensitivity reactions.
Possible systemic adverse effects.

**3.2 Paediatric use:** Children > 12 years.

**4. COMMENTS/REFERENCES**

**References:**
Martindale: The Complete Drug Reference, 35th and 37th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Tromantadine

**1.2 ATC Code:** D06BB02 Chemotherapeutics for topical use, Antivirals

**1.3 Therapeutic indications:** Treatment of herpes simplex infections of the skin and mucous membranes and of herpes zoster.

**1.4 Posology and duration of treatment:** 3 times daily; if no improvement occurs after 2 days of treatment, treatment should be stopped.

**1.5 Pharmaceutical forms:** 0.1% gel.

**1.6 Contraindications (SmPC):** Hypersensitivity; not if blisters are fully formed.

**1.7 Relevant warnings (SmPC):** Contact dermatitis has been reported after the topical use of tromantadine hydrochloride.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance)**: Application site reactions and, rarely, super-infection or abscesses.

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | OTC see Annex III | | | | | |
| Publication** | OTC see Annex III | | | | | |
| A | Not authorised | | | | | |
| B | Not authorised | | | | | |
| CZ | OTC see Annex III | | | | | |
| E | I | | | | | |
| F | Not authorised | | | | | |
| HR | Not authorised | | | | | |
| I | POM | | | | | |
| LV | OTC see Annex III | | | | | |
| MK | I | | | | | |
| P | OTC see Annex III | | | | | |
| PL | OTC see Annex III | | | | | |
| RO | Not authorised | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/
** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: OTC see Annex III**

**3.2 Paediatric use:** No data

## 4. COMMENTS/REFERENCES

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Tyrothricin

**1.2 ATC Code:** D06AX08 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** It is active *in vitro* against many Gram-positive bacteria and has been used either alone or with other anti-bacterials in the localised treatment of infections (mainly of the skin and mouth).

**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):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** Tyrothricin is too toxic to be used systemically; effects that have been reported include liver and kidney damage, as well as Stevens-Johnson syndrome. It damages the sensory epithelium of the nose and instances of prolonged loss of smell have occurred after its use as a nasal spray or instillation. Tyrothricin should not be instilled into the nasal cavities or into closed body cavities.

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

| Country | Prescription status | Exemptions | | | | |
|---|---|---|---|---|---|---|
| | | Routes of administration | Comments | MS | MDD | MQP |
| Melclass database* | I | | | | | |
| Publication** | I | | | | | |
| A | Not authorised as mono-product | | | | | |
| CH | Deleted | | | | | |
| CZ | Not authorised | | | | | |
| D | OTC see Annex III | | | | | |
| F | Not authorised | | | | | |
| H | I | | Suspended for 6 months | | | |
| HR | OTC see Annex III | | Gel | 0.1% | | 100g |
| I | OTC see Annex III | | | | | |
| LT | OTC see Annex III | | | | | |
| MK | Not authorised | | | | | |
| NL | Not authorised | | | | | |
| P | Not authorised | | | | | |
| PL | Not authorised | | | | | |
| RO | I | | | | | |

* Melclass database - Available at: http://www.edqm.eu/melclass/

** Revisions of the appendices of Resolution ResAP (2007)1 - Available at: http://go.edqm.eu/PHO

No data available from other member states.

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

**Recommendation: List I**

**3.2 Paediatric use:** No data.

**4. COMMENTS/REFERENCES**

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

## 1. THERAPEUTIC PROFILE

**1.1 Active ingredient:** Virginiamycin

**1.2 ATC Code:** D06AX10 Antibiotics for topical use, Other antibiotics for topical use

**1.3 Therapeutic indications:** Virginiamycin is a streptogramin anti-bacterial mixture principally consisting of two anti-microbial substances, virginiamycin $M_1$ and virginiamycin $S_1$, produced by the growth of *Streptomyces virginiae*. It has been used for the treatment of infections due to sensitive organisms, particularly Gram-positive cocci.

**1.4 Posology and duration of treatment:** -

**1.5 Pharmaceutical forms: -**

**1.6 Contraindications:** -

**1.7 Relevant warnings (SmPC):** It may cause gastrointestinal disturbances including diarrhoea and vomiting. A few instances of hypersensitivity have been observed.

## 2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

**2.1 Direct risks (Pharmacovigilance):** -

**2.1.1 Recent cases at European level:** -

**2.1.2 Indirect risks (incorrect use):** -

## 3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: No data in *melclass* database.

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

**Recommendation: Not to classify**

## 4. COMMENTS/REFERENCES

Virginiamycin has been used in animal feedstuffs as a growth promoter.

**References:**

Martindale: The Complete Drug Reference, 35th edition.
Drug Information by: Micromedex - Thomson Healthcare Inc. Last updated 1 February 2012 (Available at: http://www.micromedexsolutions.com).
Drug Information Online (Available at: http://www.drugs.com).
Electronic Medicines Compendium (eMC) (Available at: http://www.medicines.org.uk/emc/).
PDR online 2012 (Available at: http://www.pdr.net/).

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