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

Evidence-based classification reviews of
medicines belonging to the ATC group R01
(Nasal preparations)

2019

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INTRODUCTION

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

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

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

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

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

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

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

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

It is important to note that:

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

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

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

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

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

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

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

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

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

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

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

DISCLAIMER

This document is published for information only.

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

They reflect the debates and conclusions of the reviews of scientific classifications of medicines that took place at the 2018-2019 meetings of the CD-P-PH/PHO. The document was reviewed and endorsed by the CD-P-PH/PHO at its 67th meeting (December 2019).

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

GLOSSARY OF TERMS USED IN THIS DOCUMENT

AGEP	Acute generalised exanthematous pustulosis
ATC	Anatomical Therapeutic Chemical classification[1]
CNS	Central nervous system
CSCR	Central serous chorioretinopathy
EDQM	European Directorate for the Quality of Medicines and HealthCare
EMA	European Medicines Agency
GI	Gastrointestinal
GSL	General sales list medication
HPA	Hypothalamo-pituitary-adrenal
MAOI	Monoamine oxidase inhibitor
MDD	Maximal daily dose
MQP	Maximal quantity per pack
MS	Maximal strength
P	Pharmacy-only medicine
POM	Prescription-only medicine
RIMA	Reversible inhibitors of monoamine oxidase A
SmPC	Summary of product characteristics
WHO	World Health Organization

Classification used throughout this document

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

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

1. Active substances in medicines subject to prescription

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

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

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

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

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

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

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Cyclopentamine

1.2 ATC code: R01AA02

1.3 Therapeutic indications: cyclopentamine is a sympathomimetic alkylamine, classified as a vasoconstrictor and formerly used as a nasal decongestant. Cyclopentamine was indicated in the past as an over-the-counter medication for use as a nasal decongestant, notably in Europe and Australia, but has now been largely discontinued.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

The DrugBank database - https://www.drugbank.ca

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Ephedrine

1.2 ATC code: R01AA03

1.3 Therapeutic indications: ephedrine salts are used in the symptomatic relief of nasal congestion. Nasal drops or sprays usually containing ephedrine 0.5 or 1% are used in the treatment of nasal congestion.

1.4 Posology and duration of treatment: ephedrine-containing products are used intranasally. One or two drops should be instilled into each nostril. Adults, elderly and children over 12: as required, but not more than 4 times a day.

1.5 Pharmaceutical forms: nasal drops, solution 0.5%; nasal drops, solution 1%; nasal drops, solution 2%.

1.6 Contraindications: ephedrine should not be given to patients who are being treated with monoamine oxidase inhibitors (MAOIs), or within 2 weeks of stopping such treatment. Ephedrine should not be taken with beta-blockers. It should be used with caution in patients receiving halogenated anaesthetics. Ephedrine nasal drops should not be used concomitantly with other sympathomimetic decongestants. It should also be avoided in patients with cardiovascular disease, cardiac arrhythmias, cardiomyopathy and peripheral vascular disease, hypertension, hyperthyroidism, hyperexcitability, phaeochromocytoma, closed-angle glaucoma and urinary retention. Ephedrine nasal drops should not be used after nasal or sinus surgery. Excessive and/or frequent use of a nasal decongestant should be avoided. Ephedrine should not be given to children under 12 years of age.

1.7 Relevant warnings: ephedrine should be used with care in the elderly and in patients with prostatic hypertrophy, diabetes mellitus or renal impairment. Long-term use of the product in hyperactive patients should be avoided. Tachyphylaxis can occur within a few days after starting the product. After long-term use, tolerance and addiction have been observed.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): adverse effects may be minimised by avoiding prolonged or excessive use.

Metabolism and nutrition disorders: hyperglycaemia, hypokalaemia.

Psychiatric disorders: hallucinations, paranoia.

Nervous system disorders: anxiety, restlessness, irritability, tremors, headache, tolerance, dependence, insomnia, dizziness and fainting.

Eye disorders: mydriasis.

Cardiac disorders: palpitations, arrhythmias.

Vascular disorders: hypertension (vasoconstriction with hypertension), vasodilation with hypotension, flushing, impaired circulation to the extremities.

Respiratory, thoracic and mediastinal disorders: dyspnoea.

Gastrointestinal (GI) disorders: nausea, thirst, dry mouth, anorexia, vomiting, increased salivation.

Skin and subcutaneous tissue disorders: sweating, dermatitis, piloerection.

Musculoskeletal and connective tissue disorders: muscular weakness.

Renal and urinary disorders: difficulty in micturition in patients with prostatic enlargement, urinary retention.

General disorders and administration site conditions: local irritation, dryness, pain, rebound congestion and drug-induced rhinitis.

2.2 Indirect risks (incorrect use): at doses much greater than recommended or in the case of particularly sensitive people, ephedrine may cause excessive nervous excitability, as well as an increase in blood pressure, increased heart rate, anxiety and insomnia, convulsions, urinary retention and dizziness. Prolonged intranasal use of ephedrine may cause chronic congestion of nasal mucosa. Paranoid psychosis, delusions and hallucinations may follow overdosage. Although illicit use of ephedrine is mainly in the manufacture of street stimulants such as methamphetamine, there is increasing evidence of the abuse of ephedrine preparations in some countries, and the public health and social problems associated with its abuse appear to be significant, particularly in certain African countries. Adverse effects reported with illicit ephedrine use include cardiovascular toxicity and chest pain.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
Armenia (AM)	Not authorised				
Austria (AT)	Not authorised				
Belgium (BE)	Not authorised				
Bosnia and Herzegovina (BiH)	Not subject to prescription		10 mg/mL		90 mg/9 mL
Switzerland (CH)	Not authorised				
Czech Republic (CZ)	Not authorised				
Germany (DE)	Not authorised				
Estonia (EE)	Not authorised				
Spain (ES)	Not authorised				
Finland (FI)	Not authorised				
Georgia (GE)	Not authorised				
Croatia (HR)	Not authorised				
Hungary (HU)	Not authorised				
Ireland (IE)	Not authorised				
Italy (IT)	Not authorised				
Lithuania (LT)	Not authorised				
Latvia (LV)	Not authorised				
North Macedonia (MK)	Not authorised				
Netherlands (NL)	Not authorised				
Poland (PL)	POM				
Portugal (PT)	Not authorised				
Romania (RO)	Not subject to prescription		1%		
Serbia (RS)	Not authorised				
Sweden (SE)	Not authorised				

Slovenia (SI)	Not authorised				
United Kingdom (UK)	Not subject to prescription (P)	Contraindicated in children < 12 years	1%		

No more data available from other member states.

Melclass database[1]: List II + Exemption (exemptions: nasal use; MS: 2%).

3.2 Social dimension of classification:

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

Proposed recommendation: **List II + Exemption**

Exemptions: nasal use; MS: 1%; MQP: 180 mg; contraindicated in children < 12 years of age.

Criteria: the use of medicines containing ephedrine as active substance is well established and authorised products are mainly available as non-prescription (see table above). Because of the potential for abuse, and to reduce the risk of misuse, the MQP should be limited to 180 mg for non-prescription medicines.

3.2.2 Paediatric use: contraindicated for children under 12 years of age.

3.2.3 Social dimension: potential for abuse: between 2007 and 2008 the UK Medicines and Healthcare products Regulatory Agency (MHRA) introduced restrictions on use of pseudoephedrine and ephedrine because of concern that medicines containing these active substances could be used in the illicit manufacture of the Class A controlled drug methylamphetamine. The following sales restrictions have been in place in the UK to manage the risk of misuse of pseudoephedrine and ephedrine: a) it is illegal to sell or supply any product that contains more than 720 mg pseudoephedrine or 180 mg ephedrine without a prescription; b) it is illegal to sell or supply a combination of products that between them add up to more than 720 mg pseudoephedrine or 180 mg ephedrine without a prescription; c) it is illegal to sell or supply a product that contains pseudoephedrine and a product that contains ephedrine in one transaction; d) furthermore, the Royal Pharmaceutical Society advises that the sale and supply of these products must be made by a pharmacist or suitably trained pharmacy staff under the supervision of a pharmacist.

4. REFERENCES/COMMENTS

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

Medicinal Products Registry Poland - http://pub.rejestrymedyczne.csioz.gov.pl

World Health Organization (WHO). Recommendations from the Expert Committee on Drug Dependence. WHO Drug Info 1998; 12: 227–229

MHRA (UK) - http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1465535195811.pdf

MHRA (UK) - Pseudoephedrine and ephedrine: update on managing risk of misuse - https://www.gov.uk/drug-safety-update/pseudoephedrine-and-ephedrine-update-on-managing-risk-of-misuse

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Phenylephrine

1.2 ATC code: R01AA04

1.3 Therapeutic indications: phenylephrine and its salts are most commonly used for the symptomatic relief of nasal congestion.

1.4 Posology and duration of treatment: for nasal congestion, a 0.25 to 1% solution may be instilled as nasal drops or a spray into each nostril every 4 hours as required. Treatment with phenylephrine should not exceed 5 days.

1.5 Pharmaceutical forms: nasal drops, solution 2.5 mg/mL; nasal drops, solution 5 mg/mL; nasal spray.

1.6 Contraindications: -

1.7 Relevant warnings: general cautions: diabetes mellitus; hypertension; hyperthyroidism. Specific cautions: with intranasal use: excessive or prolonged use should be avoided; cardiovascular disease.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): phenylephrine has mainly alpha-agonist effects. It has a longer duration of action than noradrenaline and an excessive vasopressor response may cause a prolonged rise in blood pressure. It induces tachycardia or reflex bradycardia and should therefore be avoided in severe hyperthyroidism and used with caution in severe ischaemic heart disease. Patients with diabetes mellitus or prostatic hyperplasia should also avoid phenylephrine. Excessive or prolonged use of phenylephrine nasal drops can lead to rebound congestion.

2.2 Indirect risks (incorrect use): overdose with phenylephrine may cause irritability, headache, increased blood pressure and reflex bradycardia.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not authorised				
BE	Not authorised				
BiH	Not authorised				
CH	Not authorised				
CZ	Not authorised				
DE	Not authorised				
ES	Not subject to prescription				
FI	Not authorised				
HR	Not authorised				
IE	Not authorised				
IT	Not subject to prescription				
LT	Not authorised				
LV	Not authorised				
MK	Not authorised				

NL	Not authorised				
PL	Not authorised				
PT	Not subject to prescription		5 mg/mL		75 mg
RS	Not authorised				
SE	Not authorised				
SI	Not authorised				

No more data available from other member states.

Melclass database[1]: currently not available.

3.2 Social dimension of classification:

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

Proposed recommendation: **Not subject to prescription**

Criteria: the use of medicines containing phenylephrine as active substance is well established and authorised products are available as non-prescription in member states (see table above). Conditions or symptoms for which the product is indicated can be correctly diagnosed without medical supervision.

3.2.2 Paediatric use: 1-2 drops should be administered up to 4 times a day as required for a maximum of 7 days, to be instilled into each nostril, administer ephedrine 0.5% nasal drops.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference - 35th and 37th Edition

British National Formulary for Children (BNF) for children

National Authority of Medicines and Health Products (INFARMED) Portugal - http://app7.infarmed.pt/infomed/download_ficheiro.php?med_id=5960&tipo_doc=rcm

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Oxymetazoline

1.2 ATC code: R01AA05

1.3 Therapeutic indications: the symptomatic relief of congestion of the upper respiratory tract due to the common cold, hay fever and sinusitis.

1.4 Posology and duration of treatment: spray and drops (0.05%): adults and children over 12 years: 1-2 sprays per nostril every 6-8 hours.

Spray and drops (0.025%): children between 6 and 12: 1-2 sprays, 2-3 times daily.

If symptoms worsen or do not improve after 3-5 days, physician should re-evaluate clinical situation. Patients are advised to use for a maximum of 7 consecutive days to avoid rebound effect and drug-induced rhinitis.

1.5 Pharmaceutical forms: nasal spray, solution; nasal drops, solution; nasal gel. Strengths: 0.01%, 0.025% and 0.05%.

1.6 Contraindications: inflammation or lesions of the skin around the nostrils or nasal mucosa; transsphenoidal hypophysectomy or nasal surgery exposing the dura mater; concomitant use of other sympathomimetic decongestants; phaeochromocytoma; patients currently taking MAOIs or who have taken MAOIs in the last 14 days.

1.7 Relevant warnings: a physician should be consulted before taking this medicine in case of: a) high blood pressure, heart disease including angina, diabetes mellitus, hyperthyroid disease, hepatic or renal disorders and prostatic hypertrophy; b) patients currently taking MAOIs or who have taken MAOIs in the last 14 days; c) occlusive vascular disease; d) patients who have narrow-angle glaucoma. If any of the following occur, treatment should be stopped: hallucinations; restlessness; sleep disturbances. Patients are advised to use for a maximum of 7 consecutive days to avoid rebound effect and drug-induced rhinitis.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): rare: eye disorders: eye irritation, dryness, discomfort or redness; Respiratory: discomfort or irritation in the nose, mouth or throat; sneezing.

Very rare: cardiovascular: tachycardia, palpitations, increased blood pressure; Central nervous system (CNS): insomnia, nervousness, tremor, anxiety, restlessness, irritability, headache; gastrointestinal: nausea.

Prolonged and/or heavy use of oxymetazoline may lead to reduced effect and/or rebound congestion (rhinitis medicamentosa), cardiovascular effects and CNS effects.

2.2 Indirect risks (incorrect use): the symptoms of moderate or acute overdosage can include mydriasis, nausea, cyanosis, fever, tachycardia, cardiac arrhythmia, hypertension, dyspnoea and cardiovascular failure. CNS depression with symptoms such as decreased body temperature, bradycardia, hypotension, apnoea or loss of consciousness is possible.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not subject to prescription	Symptomatic treatment of nasal congestion.	0.5 mg/mL	2-3 times daily	30 mL
AT	List II + Exemption	Ex.: treatment of nasal mucosa List II for children under 6			
BE	Not subject to prescription				
BiH	Not subject to prescription				
CH	Not subject to prescription				
FI	Not authorised				
HR	Not subject to prescription	Symptomatic relief of congestion of the upper respiratory tract due to the common cold, hay fever and sinusitis. For diagnostic uses.	0.5 mg/mL	2 drops 3 times per day into each nostril	10 mL (5 mg)
IE	Not subject to prescription	Symptomatic relief of acute rhinitis in allergic or upper respiratory tract infection, including the common cold or influenza	0.05%	Two sprays (0.05 g per spray) per nostril every 6-8 hours	15 mL
IT	Not subject to prescription				
LT	Not subject to prescription				
MK	Not subject to prescription				
PL	Not subject to prescription	Symptomatic relief of nasal congestion due to hay fever, common cold and sinusitis	0.5 mg/mL = 0.05%	It depends on form and strengths	50 mg
PT	Not subject to prescription	All situations in which congestion occurs, nasal disorders such as rhinitis, sinusitis	0.5 mg/mL		7.5 mg
RS	Not subject to prescription	For the fast relief of stuffy noses due to head colds and hay fever.	0.05%		10 mL

No more data available from other member states.

Melclass database[1]: Not subject to prescription.

3.2 Social dimension of classification:

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

Proposed recommendation: **Not subject to prescription** (adults and children over 6 years of age; no longer than 5 days; for children < 6 years of age doctor's advice needed).

Criteria: the use of medicines containing oxymetazoline as active substance is well established and authorised products are available as non-prescription in member states. Conditions or symptoms for which the product is indicated can be correctly diagnosed without medical supervision.

3.2.2 Paediatric use: in early 2009, the MHRA advised that non-prescription cough and cold preparations should not be given to children under 6 years of age as there was no robust evidence of their efficacy and because they can cause adverse effects such as allergic reactions, sleep disturbances and hallucinations. In those aged from 6 to 12 years, such preparations should only be used as second-line therapy and for no more than 5 days; the MHRA also considered that further research is warranted in this age group.
3.2.3 Social dimension: -

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

4. REFERENCES/COMMENTS

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

British National Formulary for Children

Medicines and Medical Devices Agency of Serbia (ALIMS) - https://www.alims.gov.rs/ciril/files/lekovi/smpc/515-01-01155-14-001.pdf

MHRA (UK) - http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1514525905036.pdf and https://www.gov.uk/drug-safety-update/over-the-counter-cough-and-cold-medicines-for-children

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Tetryzoline

1.2 ATC code: R01AA06

1.3 Therapeutic indications: it is used as the hydrochloride for its vasoconstrictor effect in the symptomatic relief of nasal congestion.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: based on the available data, medications containing tetryzoline are authorised in Italy (classification status: not subject to prescription). No medications containing this active substance are authorised in the rest of the member states.

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Italian Medicines Agency (AIFA) - https://bit.ly/2TAKRJk

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Xylometazoline

1.2 ATC code: R01AA07

1.3 Therapeutic indications: treatment of nasal congestion, perennial and allergic rhinitis (including hay fever), sinusitis.

1.4 Posology and duration of treatment: adults, children over 12 years and the elderly (0.1%): one application in each nostril 2 or 3 times daily. Children between 6 and 12 years (0.05%): 1 or 2 applications in each nostril 1 or 2 times daily. Not to be used for more than 5 days without the advice of a doctor.

1.5 Pharmaceutical forms: nasal spray, solution; nasal drops, solution. Strengths: 0.05%; 0.1%

1.6 Contraindications: concomitant use of other sympathomimetic decongestants; cardiovascular disease including hypertension; diabetes mellitus; phaeochromocytoma; hyperthyroidism; closed-angle glaucoma; MAOIs (or within 14 days of stopping treatment); beta-blockers; inflammation of the skin and/or mucosa of the nasal vestibule; transsphenoidal hypophysectomy or nasal surgery exposing the dura mater. Not to be used in children under the age of 6 years.

1.7 Relevant warnings: patients are advised not to take decongestants for more than 5 consecutive days. Xylometazoline, like other preparations belonging to the same class of active substances, should be used only with caution in patients showing a strong reaction to sympathomimetic agents as evidenced by signs of insomnia, dizziness, etc. Medicines containing xylometazoline should not be used continuously for more than 5 consecutive days. If symptoms persist, patients should consult their doctor. Occasionally small children may show restlessness or sleep disturbance when xylometazoline is used. If this occurs use of xylometazoline should be stopped.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): the following side effects have occasionally been encountered: a burning sensation in the nose and throat, local irritation, nausea, headache and dryness of the nasal mucosa. Systemic cardiovascular effects have occurred and this should be kept in mind when giving xylometazoline to people with cardiovascular disease. In isolated cases, systemic allergic reactions and transient visual disturbances.

2.2 Indirect risks (incorrect use): in rare instances of accidental poisoning in children, the clinical picture has been marked chiefly by signs such as acceleration and irregularity of the pulse, elevated blood pressure and sometimes consciousness clouding.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not subject to prescription	For the symptomatic relief of nasal congestion, perennial and allergic rhinitis (including hay fever), sinusitis.	1 mg/mL	3 times daily	15 mL
AT	List II + Exemption	Ex.: treatment of rhinitis	Ex.: 0.09 mg in each nostril	Ex.: 0.27 mg in each nostril	N.A.
BE	Not subject to prescription	Short symptomatic treatment of nasal congestion			

BiH	Not subject to prescription	Symptomatic relief of nasal congestion, perennial and allergic rhinitis, sinusitis	1 mg/mL		
CH	Not subject to prescription				
DE	Not authorised				
GE	Not subject to prescription				
HR	Not subject to prescription	For the symptomatic relief of nasal congestion, perennial and allergic rhinitis (including hay fever), sinusitis.	1 mg/mL	One application in each nostril up to 3 times daily	15 mL (15 mg)
IE	Not subject to prescription (P)	Temporary symptomatic treatment of nasal congestion due to rhinitis or sinusitis. This medicine should be used for a maximum of 7 days Contraindicated in children less than 12 years of age	0.1% (1 mg/mL)	One spray into each nostril not more often than 3 times per day.	10 mL
IT	Not subject to prescription				
LT	Not subject to prescription				
MK	Not subject to prescription	Allergic rhinitis, sinusitis, acute otitis media	1 mg/mL	1.2 mg	10 mL
PL	Not subject to prescription	Treatment of nasal congestion, perennial and allergic rhinitis (including hay fever) and sinusitis. No longer than 7 days. Nasal drops, nasal aerosols and nasal gels 0.05%, and 0.1%; strength 0.05% is applicable for children > 2 years.	0.1% = 1 mg/mL	0.54 mg	10 mg
PT	Not subject to prescription	All situations in which congestion occurs, nasal disorders such as rhinitis, sinusitis	0.5 mg/mL		7.5 mg
RO	Not subject to prescription				
RS	Not subject to prescription	For the symptomatic relief of nasal congestion, perennial and allergic rhinitis (including hay fever), sinusitis. 0.1% - for adults and children over 12; 0.05% - for children between 6 and 12 years	0.1%		10 mL

No more data available from other member states.

Melclass database[1]: not subject to prescription (route of administration: nasal use; indications: symptomatic relief of nasal congestion, perennial and allergic rhinitis (including hay fever), sinusitis).

3.2 Social dimension of classification:

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

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

Proposed recommendation: **Not subject to prescription** (adults and children over 6 years of age; no longer than 5 days; for children < 6 years of age doctor's advice needed).

Criteria: conditions or symptoms for which the product is indicated can be correctly diagnosed without medical supervision.

3.2.2 Paediatric use: not for children under 6 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

British National Formulary for Children

ALIMS - https://www.alims.gov.rs/ciril/files/lekovi/smpc/515-01-5642-12-001.pdf

MHRA - http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1471583032275.pdf and https://www.gov.uk/drug-safety-update/over-the-counter-cough-and-cold-medicines-for-children

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Naphazoline

1.2 ATC code: R01AA08

1.3 Therapeutic indications: symptomatic relief of nasal congestion related to rhinitis and rhinosinusitis.

1.4 Posology and duration of treatment: adults: 2-3 drops in each nostril every 4-6 hours. Children over 6: naphazoline nitrate 0.05% has been applied topically as nasal drops or a spray, usually 2 or 3 times daily, in children aged 6 years and over for the symptomatic relief of nasal congestion. Duration of treatment: short-term use, 3-5 days.

1.5 Pharmaceutical forms: nasal drops, solution, 0.5 mg/mL; nasal drops, solution, 0.1 mg/mL.

1.6 Contraindications: closed-angle glaucoma; MAOIs (or within 14 days of stopping treatment); inflammation of the skin and/or mucosa of the nasal vestibule; transsphenoidal hypophysectomy or nasal surgery exposing the dura mater.

1.7 Relevant warnings: this medicine should only be used after careful consideration of the benefits and risks in the following groups of patients: treatment with medicines that possibly lead to an increase in blood pressure; severe cardiovascular diseases (e.g. coronary heart disease, hypertension); phaeochromocytoma; porphyria; metabolic disorders (e.g. hyperthyroidism, diabetes); prostatic hyperplasia. The prescribed dose should not be exceeded. The drug should not be used for more than 5 consecutive days in order to avoid a rebound phenomenon, or drug-induced rhinitis. If after 3-5 days the symptoms persist or if there is a deterioration or occurrence of new symptoms, the drug should be discontinued. Long-term use and overdose of sympathomimetic nasal decongestants can lead to reactive hyperaemia of the mucous membrane of the nose. A doctor or pharmacist should ensure that the patient does not take multiple preparations containing sympathomimetics at the same time (both for oral and topical use).

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): naphazoline can cause local hypersensitivity or mucosal congestion. For high-dose treatments or for therapies lasting more than 4 consecutive days the naphazoline absorbance through the inflamed mucosae can cause systemic effects such as hypertension, bradycardia, cephalalgy and micturition difficulties.

2.2 Indirect risks (incorrect use): in case of overdose, where naphazoline has been accidentally orally ingested, it can cause arterial hypertension, bradycardia, serious cephalalgy, and in children hypothermia and CNS depression with high sedation.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not subject to prescription		1 mg/mL	3-4 times daily	10 mL
AT	List II + Exemption	Exemption for eye preparations up to 0.1% and nasal application. POM for children under 6	Ex.: 0.1% (eye preparations)		

BE	Not subject to prescription	Short symptomatic treatment of nasal congestion			
BiH	Not subject to prescription	Temporary relief of stuffy nose due to rhinitis and rhinosinusitis	1 mg/mL		
CH	Not authorised				
DE	Not subject to prescription				
GE	Not subject to prescription				
HR	Not subject to prescription	Symptomatic relief of nasal congestion related to rhinitis and sinusitis.	1 mg/mL	2-3 drops in each nostril every 4-6 hours	10 mL
IE	Not authorised				
IT	Not subject to prescription				
LT	Not authorised				
MK	Not subject to prescription		1 mg/mL	0.8 mg	10 mL
PL	Not subject to prescription	Symptomatic treatment of acute and chronic rhinitis and sinusitis. No longer than 3 - 5 days; children > 6 years	1 mg/mL = 0.1%	2-4 drops every 4-6 hours	10 mg
PT	Not authorised				
RO	Not subject to prescription				
RS	Not subject to prescription	Fast relief of stuffy nose due to rhinitis and rhinosinusitis. 0.1% - for adults; 0.05% - for children over 7	0.1%		10 mL

No more data available from other member states.

Melclass database[1]: Not subject to prescription.

3.2 Social dimension of classification:

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

Proposed recommendation: **Not subject to prescription** (nasal use; adults and children > 6 years of age; short-term use (5 days); for children < 6 years of age doctor's advice needed).

Criteria: conditions or symptoms for which the product is indicated can be correctly diagnosed without medical supervision.

3.2.2 Paediatric use: not for children under 6 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

ALIMS - https://www.alims.gov.rs/ciril/files/lekovi/smpc/515-01-9043-12-001.pdf

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

4.2 Comments: medicines containing naphazoline for ophthalmological use are under a different ATC code (ATC: S01GA01).

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Tramazoline

1.2 ATC code: R01AA09

1.3 Therapeutic indications: tramazoline is used to provide symptomatic relief of nasal congestion.

1.4 Posology and duration of treatment: tramazoline is used in adults, adolescents and children over 6 years. Tramazoline hydrochloride is given as a solution containing about 0.12%, instilled into each nostril as nasal drops or a spray 3 or 4 times daily. Due to the risk of atrophy of the nasal mucosa, this medicinal product must not be used for more than 7 days.

1.5 Pharmaceutical forms: nasal drops and nasal spray, solution 0.12%.

1.6 Contraindications: closed-angle glaucoma; transsphenoidal hypophysectomy or nasal surgery exposing the dura mater; rhinitis sicca; children under 6 years.

1.7 Relevant warnings: prolonged use of decongestants such as tramazoline may lead to the development of tolerance with chronic swelling (resulting in a permanent nasal congestion) and eventually to atrophy of the nasal mucosa. Tramazoline should only be used with caution and with medical advice because of the risk of systemic absorption in patients with: arterial hypertension; heart disease; vascular diseases; hyperthyroidism; diabetes mellitus; phaeochromocytoma; prostatic hypertrophy; hyperglycaemia; porphyria.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): Immune system disorders: not known: hypersensitivity reactions.

Psychiatric disorders: uncommon: restlessness; not known: hallucinations, insomnia.

Nervous system disorders: uncommon: headache; rare: dizziness, dysgeusia; not known: somnolence, sedation.

Cardiac disorders: uncommon: palpitations; not known: tachycardia, arrhythmia.

Respiratory, thoracic and mediastinal disorders: common: local irritation of the nasal mucosa; uncommon: dryness of the nasal mucosa, sneezing, rhinorrhoea, swelling of the nasal mucosa; rare: epistaxis.

GI disorders: uncommon: nausea.

2.2 Indirect risks (incorrect use): overdose or frequent repeated use may result in dryness of the nasal mucosa resulting in a recurrence of mucous membrane swelling (rebound effect), as well as chronic rhinitis and mucosal necrosis. In case of accidental local overdose or inadvertent ingestion the following symptoms may occur: dizziness, vomiting, mydriasis, miosis, sweating, pallor, cyanosis of the lips, fever, seizures, cardiovascular disorders (hypertension, tachycardia, arrhythmia), cardiac arrest, pulmonary oedema, respiratory disorders including respiratory depression and respiratory arrest, psychiatric disorders.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	List II + Exemption	Treatment of nasal mucosa swelling in allergic and non-allergic rhinitis Exemption for nasal application, POM for children under 6	0.089 mg in each nostril	0.356 mg in each nostril	
BE	Not subject to prescription	Short symptomatic treatment of nasal congestion			
BiH	Not authorised				
CH	Not authorised				
DE	Not subject to prescription				
GE	Not authorised				
HR	Not authorised				
IE	Not authorised				
IT	Not subject to prescription				
LT	Not authorised				
MK	Not authorised				
PL	Not authorised				
PT	Not subject to prescription	For the relief of nasal congestion	1.18 mg/mL		10 mL (11.8 mg)
RO	Not subject to prescription				
RS	Not authorised				

No more data available from other member states.

Melclass database[1]: Not subject to prescription.

3.2 Social dimension of classification

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

Proposed recommendation: **Not subject to prescription** (nasal use; adults and children > 6 years of age; short-term use (5 days); for children < 6 years of age doctor's advice needed).

Criteria: conditions or symptoms for which the product is indicated can be correctly diagnosed without medical supervision.

3.2.2 Paediatric use: not for children under 6 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

Austrian Medicines and Medical Devices Agency (AGES) - SmPC Rhinospray® plus ätherische Öle -

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

Nasenspray.

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Metizoline

1.2 ATC code: R01AA10

1.3 Therapeutic indications: metizoline has been used for its vasoconstrictor activity in the treatment of nasal congestion.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Tuaminoheptane

1.2 ATC code: R01AA11

1.3 Therapeutic indications: tuaminoheptane has been used as tuaminoheptane sulfate for the symptomatic relief of nasal congestion.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fenoxazoline

1.2 ATC code: R01AA12

1.3 Therapeutic indications: fenoxazoline has been used topically for its vasoconstrictor properties in the symptomatic treatment of nasal congestion.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Tymazoline

1.2 ATC code: R01AA13

1.3 Therapeutic indications: tymazoline has been used for its local vasoconstrictor effect in the symptomatic relief of nasal congestion.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Epinephrine

1.2 ATC code: R01AA14

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Indanazoline

1.2 ATC code: R01AA15

1.3 Therapeutic indications: indanazoline has been used as indanazoline hydrochloride for its vasoconstrictor effect in the management of nasal congestion.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Phenylephrine

1.2 ATC code: R01AB01

1.3 Therapeutic indications: authorised medicinal products contain phenylephrine in combination with dimetindene. These products are indicated for the treatment of common cold symptoms, acute and chronic rhinitis and allergic rhinitis, and vasomotor rhinitis. Supportive treatment of acute and chronic sinusitis and of otitis media. Pre- and post-operative care for nose surgery.

1.4 Posology and duration of treatment: adults and children > 6 years. Nasal route: 1-2 puffs 3 to 4 times daily, for no longer than 7 days.

1.5 Pharmaceutical forms: nasal sprays, drops and gels. MS: 2.5 mg + 0.25 mg/mL (combination product: phenylephrine and dimetindene)

1.6 Contraindications: hypersensitivity to phenylephrine, dimetindene or to any of the excipients; use of MAOIs currently or within the last 14 days; trophic rhinitis; glaucoma with a narrow angle; use in children under the age of 6.

1.7 Relevant warnings: as for phenylephrine for nasal use. In addition: as dimetindene is a histamine H1 receptor antagonist, this medicinal product should be used with caution in patients with epilepsy.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): respiratory, thoracic and mediastinal disorders: rare: nose discomfort, dry nose, epistaxis.

General disorders and administration site conditions: rare: burning at the application site.

2.2 Indirect risks (incorrect use): overdose may cause sympathomimetic effects and also mild sedation, dizziness, fatigue, abdominal pain, nausea, vomiting and mild anticholinergic activity.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not subject to prescription	In combination with dimetindene	MS: 2.5 + 0.25 mg/mL		
BE	Not authorised				
BiH	Not authorised				
CH	Not subject to prescription	In combination with dimetindene			
CZ	Not subject to prescription	In combination with dimetindene			
DE	Not authorised				
EE	Not authorised				
ES	Not authorised				
FI	Not authorised				
FR	Not authorised				

HR	Not authorised				
HU	Not subject to prescription	In combination with dimetindene			
IE	Not authorised				
IT	Not authorised				
LT	Not authorised				
LV	Not subject to prescription	In combination with dimetindene			
MK	Not authorised				
NL	Not authorised				
PL	Not subject to prescription	In combination with mepyramine (MS: 2.5 + 1.5 mg/mL) In combination with dimetindene (MS: 2.5 + 0.25 mg/mL)			
PT	Not authorised				
RO	Not subject to prescription	In combination with dimetindene			
RS	Not authorised				
SE	Not authorised				
SI	Not authorised				
UK	Not authorised				

No more data available from other member states.

Melclass database[1]: Not subject to prescription.

3.2 Social dimension of classification:

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

Proposed recommendation: Phenylephrine and dimetindene: **Not subject to prescription**

Criteria: easy self-diagnosis; short-term use; systemic effect negligible during short-term treatment; not subject to prescription in most member states where authorised.

3.2.2 Paediatric use: children > 6 years of age; use in children < 6 years is not recommended.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: SmPCs for products containing combination of phenylephrine and dimetindene maleate: Otrivin Allergy® (PL: https://bit.ly/2EyuvZi), Vibrocil® nasal gel and Vibrocil® nasal drops (CZ: http://www.sukl.eu/modules/medication/search.php), Vibrocil® Nasenspray and Vibrocil® Nasentropfen (AT: https://bit.ly/2T0Qa0x); Vibrocil® nasal drops, Vibrocil® nasal spray Vibrocil® nasal gel (CH: https://bit.ly/2F4ofIY)

4.2 Comments: there is another combination product authorised in Poland only: phenylephrine + mepyramine maleate: classification: not subject to prescription (pharmaceutical form: nasal spray; indication: rhinitis including allergic rhinitis, vasomotor rhinitis, sinusitis (acute and exacerbation of chronic); adults and children > 6 years; MS: 1.25 +0.75 mg/mL; MDD: 8 doses daily (1 puff contains 0.25 mg + 0.15 mg respectively) and no longer than 3 days; MQP 25 mg + 15 mg (10 mL)).

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Naphazoline

1.2 ATC code: R01AB02

1.3 Therapeutic indications: authorised medicinal products contain naphazoline in combination with antazoline and in combination with diphenhydramine. These products are indicated for the treatment of acute rhinitis, exacerbations of perennial and seasonal rhinitis or cold. Use recommended in adults and children > 6 years.

1.4 Posology and duration of treatment: different in the member states depending on the MS and specific product.

1.5 Pharmaceutical forms: nasal drops and nasal sprays.

1.6 Contraindications: hypersensitivity to antazoline, naphazoline or any of the excipients; narrow-angle glaucoma; hypersensitivity to adrenomimetic agents.

1.7 Relevant warnings: because it cannot be excluded that a small quantity of active substance could be absorbed into the blood, the product should be used with special caution in patients with coexisting cardiovascular disease, hyperthyroidism, diabetes, hypertrophy of prostate gland and in the elderly. It should not be used concomitantly with MAOIs.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): very rare: metabolism and nutrition disorders: hyperglycaemia; nervous system disorders: drowsiness, headaches and dizziness, anxiety; cardiac disorders: cardiac arrhythmia; vascular disorders: increased blood pressure; GI disorders: nausea; general disorders and conditions at the application site: weakness, excessive sweating.

2.2 Indirect risks (incorrect use): no data are available on acute overdose of topical nasal drops. Prolonged or too frequent administration of the product in children, or accidental oral intake, may lead to inhibition of the CNS, hypothermia and even coma. Naphazoline may cause a sudden decrease in blood pressure, tachycardia.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	List II + Exemption	Ex.: in combination with diphenhydramine and for nasal application			
BE	Not authorised				
BiH	Not authorised				
CH	Not authorised				
CZ	Not subject to prescription	In combination with antazoline			
DE	Not authorised				
EE	Not authorised				
ES	Not authorised				
FI	Not authorised				

FR	Not authorised				
GE	Not subject to prescription				
HR	Not authorised				
HU	Not subject to prescription				
IE	Not authorised				
IT	Not authorised				
LT	Not authorised				
LV	POM	In combination with diphenhydramine			
MK	Not authorised				
NL	Not authorised				
PL	Not subject to prescription	In combination with diphenhydramine, antazoline, and sulfathiazole			
PT	Not authorised				
RO	Not authorised				
RS	Not authorised				
SE	Not authorised				
SI	Not authorised				
UK	Not authorised				

No more data available from other member states.

Melclass database[1]: List II + Exemption (exemption: nasal use).

3.2 Social dimension of classification:

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

Proposed recommendation: combination with naphazoline: **Not subject to prescription**; combination with diphenhydramine: **Not subject to prescription**.

Criteria: easy self-diagnosis; short-term use; systemic effect negligible during short-term treatment; not subject to prescription in most member states where authorised.

3.2.2 Paediatric use: children > 6 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Rhinophenazol® (PL: https://bit.ly/2EyuvZi) and Betadrin WZF® (PL: https://bit.ly/2EyuvZi)

4.2 Comments: there is another combination product authorised in Poland only: naphazoline + sulfathiazole: classification: not subject to prescription (indication: acute bacterial rhinitis; adults and children > 12 years for short-term use (no longer than 5 days); MS: 1 mg + 50 mg/mL; MDD: 0.6 mg + 30 mg; MQP 20 mg + 1000 mg (20 mL)).

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Tetryzoline

1.2 ATC code: R01AB03

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Ephedrine

1.2 ATC code: R01AB05

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: based on the available data, a combination product containing ephedrine and silver protein is authorised in Austria (classification status: List II), and a combination product containing ephedrine and neomycin is authorised in Romania (classification status: not subject to prescription). No medications containing ephedrine are authorised in the rest of the member states.

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, medicines containing ephedrine are not authorised in at least 3 member states: **Not to classify**.

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Xylometazoline

1.2 ATC code: R01AB06

1.3 Therapeutic indications: authorised medicinal products contain xylometazoline and dexpanthenol, and xylometazoline and ipratropium bromide.

Xylometazoline and dexpanthenol: to reduce swelling of the nasal mucosa in rhinitis and as supportive treatment for healing of mucocutaneous lesions, paroxysmal rhinorrhoea (vasomotor rhinitis) and for the treatment of obstructed nasal breathing after surgery on the nose (dexpanthenol protects the epithelium and promotes wound healing. Xylometazoline facilitates nasal breathing due to decongestion and improved mucus drainage*)*.

Xylometazoline and ipratropium bromide: symptomatic treatment of nasal congestion and rhinorrhoea in connection with common colds.

1.4 Posology and duration of treatment: xylometazoline and dexpanthenol: one spray 3 times daily into each nostril. MS: 1 mg + 50 mg/mL; MDD to one nostril 0.03 mg + 15 mg; MQP 30 mg + 1500 mg (30 mL). No longer than 7 days.

Xylometazoline and ipratropium bromide: one puff in each nostril up to 3 times daily. At least 6 hours should elapse between 2 doses. MS: 0.5 mg + 0.6 mg/mL; MDD: 1.5 mg + 1.8 mg; MQP: 5 mg + 6 mg (10 mL). No longer than 7 days. Adults only.

1.5 Pharmaceutical forms: nasal aerosol/spray.

1.6 Contraindications: xylometazoline and dexpanthenol: hypersensitivity to the active substances or to any of the excipients; rhinitis sicca - except in the diagnostic workup to identify rhinitis sicca or atrophic rhinitis; status post transsphenoidal hypophysectomy or other surgery exposing the dura mater. MS: 0.5 mg/mL + 50 mg/mL: it must not be used in children below 2 years of age.

Xylometazoline and ipratropium bromide: hypersensitivity to the active substances or to any of the excipients; known hypersensitivity to atropine or similar substances, e.g. hyoscyamine and scopolamine; after surgical operations where dura mater may have been penetrated, e.g. transsphenoidal hypophysectomy or other transnasal operations; in patients with glaucoma; in patients with rhinitis sicca; not for children and adolescents under the age of 18 due to lack of sufficient documentation.

1.7 Relevant warnings: xylometazoline and dexpanthenol: it should be used with caution in the following conditions: patients treated with MAOIs or other medicinal products with a potentially hypertensive effect; increased intraocular pressure, especially narrow-angle glaucoma; severe cardiovascular disorders (e.g. coronary heart disease, hypertension); phaeochromocytoma; metabolic disorders (e.g. hyperthyroidism, diabetes); porphyria; prostatic hyperplasia. The effect may be attenuated particularly during prolonged use and in the event of an overdose with nasal decongestants. The following may occur as a result of misusing nasal decongestants: reactive hyperaemia of the nasal mucosa (rhinitis medicamentosa); atrophy of the nasal mucosa; use in chronic rhinitis may proceed only under medical supervision due to the risk of nasal mucosal atrophy. Other information: reactive hyperaemia of the nasal mucosa may occur, especially in the event of prolonged use and overdose of decongestant sympathomimetics. This rebound effect causes a narrowing of the airways, resulting in the repeated and even permanent use of the medicinal product by the patient. Sequelae include chronic swelling (rhinitis medicamentosa) and even atrophy of the nasal mucosa (atrophic rhinitis). In case of misuse or use of excessive amounts of the spray, the absorption of xylometazoline can cause systemic adverse effects, particularly in children (cardiovascular and neurological adverse effects).

Xylometazoline and ipratropium bromide: it must be administered with caution to patients predisposed to narrow-angle glaucoma or patients with hypertrophy of the prostate and urethral stenosis. Caution is recommended in patients predisposed to epistaxis (e.g. elderly), paralytic ileus or cystic fibrosis. It

must be used with caution in patients who are sensitive to adrenergic substances, which may give symptoms such as sleeping disturbances, dizziness, tremor, cardiac arrhythmias or elevated blood pressure. Caution is recommended in patients with hyperthyroidism, diabetes mellitus, hypertension, cardiovascular diseases or phaeochromocytoma. The treatment duration should not exceed 7 days, as chronic treatment with xylometazoline may cause swelling of the nasal mucosa and hypersecretion because of increased sensibility in the cells, “rebound effect” (rhinitis medicamentosa). Avoid spraying in or around the eye. If the drug comes into contact with the eyes, the following may occur: temporary blurred vision, irritation, pain, red eyes. Aggravation of angle-closure glaucoma may also develop.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): xylometazoline and dexpanthenol: immune system disorders: uncommon: hypersensitivity reactions (angioedema, skin rash, pruritus); psychiatric disorders: very rare: agitation, insomnia , hallucinations (especially in children); nervous system disorders: very rare: fatigue (drowsiness, sedation), headache, convulsions (especially in children); cardiac disorders: rare: palpitations, tachycardia; very rare: arrhythmia; vascular disorders: rare: hypertension; respiratory, thoracic and mediastinal disorders: very rare: increased swelling of mucous membranes after discontinuation of treatment, epistaxis.

Xylometazoline and ipratropium bromide: the most commonly reported adverse reactions are epistaxis occurring in 14.8% and nasal dryness occurring in 11.3% of patients. Many of the adverse events reported are also symptoms of common cold. Immune system disorders: not known: hypersensitivity. Psychiatric disorders: uncommon: insomnia. Nervous system disorders: common: dysgeusia, headache; uncommon: parosmia, dizziness, tremor. Eye disorders: uncommon: eye irritation, dry eye; not known: accommodation disorder, aggravation of narrow-angle glaucoma, eye pain, photopsia. Cardiac disorders: uncommon: palpitations, tachycardia. Respiratory, thoracic and mediastinal disorders: common: epistaxis, nasal dryness, nasal discomfort, nasal congestion, dry and irritated throat, rhinalgia; uncommon: nasal ulcer, sneezing, pharyngolaryngeal pain, cough, dysphonia, rhinorrhoea; not known: paranasal sinus discomfort. GI disorders: common: dry mouth; uncommon: dyspepsia, nausea; not known: dysphagia. Skin and subcutaneous disorders: not known: pruritus. Renal and urinary disorders: not known: urine retention. General disorders and administration site conditions: uncommon: discomfort, fatigue; not known: chest discomfort, thirst, systemic allergic reactions.

2.2 Indirect risks (incorrect use): xylometazoline: overdose of oral or excessive administration of topical xylometazoline may cause severe dizziness, perspiration, severely lowered body temperature, headache, bradycardia, hypertension, respiratory depression and coma. Hypertension may be followed by hypotension. Small children are more sensitive to toxicity than adults. Overdose in infants can cause serious depression of the CNS.

Dexpanthenol: pantothenic acid and its derivatives, such as dexpanthenol, have very low toxicity. No measures are required in the event of overdose.

Ipratropium bromide: the absorption being very small after nasal or oral administration, an acute overdose after intranasal ipratropium bromide is hardly possible, but if an overdosing should occur the clinical picture is dry mouth, accommodation difficulties and tachycardia. A considerable overdose may cause anticholinergic CNS symptoms such as hallucinations, which must be treated with cholinesterase inhibitors.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not subject to prescription				
AT	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide			
BE	Not subject to prescription				
BiH	Not subject to prescription	In combination with ipratropium bromide			
CH	Not subject to prescription				
CZ	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide			
DE	Not subject to prescription				
EE	Not authorised				
ES	Not subject to prescription	In combination with ipratropium bromide			
FI	Not subject to prescription				
FR	Not authorised				
GR	Not subject to prescription				
HR	POM + Exemption	Ex.: In combination with dexpanthenol			
HU	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide Nasal drops, nasal gel and nasal spray.			
IE	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide. Nasal spray for children is subject to prescription which may be renewed.			10.0 mL
IT	Not subject to prescription				
LT	Not authorised				
LV	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide			
MK	Not subject to prescription	Adults only			10 mL
NL	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide			
PL	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide			
PT	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide	0.1%		
RO	Not subject to prescription				
RS	Not subject to prescription	In combination with dexpanthenol / In combination with ipratropium bromide	0.1%		
SE	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide			
SI	Not subject to prescription	In combination with dexpanthenol/In combination with ipratropium bromide			
UK	Not subject to prescription				

No more data available from other member states.

Melclass database[1]: Currently not available.

3.2 Social dimension of classification:

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

Proposed recommendation: xylometazoline and dexpanthenol: **Not subject to prescription** (children > 2 years).

Xylometazoline and ipratropium bromide: **Not subject to prescription** (adults only).

Criteria: easy self-diagnosis; short-term treatment; systemic effect during short treatment is negligible; not subject to prescription in most member states.

3.2.2 Paediatric use: xylometazoline has been shown to be safe in children in several clinical trials. Data from clinical trials and case reports indicates that frequency, type and severity of adverse reactions in children are expected to be similar to those in adults. The majority of adverse events reported in children occurred after overdosing of xylometazoline. These include nervousness, insomnia, sleepiness/drowsiness, hallucinations and convulsions. Cases of irregular breathing have been recorded in infants and neonates.

Xylometazoline and dexpanthenol: children > 2 years. Dexpanthenol is considered as a safe ingredient.

Xylometazoline and ipratropium bromide: adult (> 18 years) use only due to lack of data.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: SmPC available in databases of national competent authorities (AT: https://bit.ly/2T0Qa0x; CH: https://bit.ly/2F4ofIY; IE: https://bit.ly/2J4I86R; PL: https://bit.ly/2EyuvZi).

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Oxymetazoline

1.2 ATC code: R01AB07

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Tuaminoheptane

1.2 ATC code: R01AB08

1.3 Therapeutic indications: authorised medicinal products contain tuaminoheptane in combination with acetylcysteine. They are indicated for short-term symptomatic treatment of nasopharyngeal diseases with excessive secretion of thick mucus.

1.4 Posology and duration of treatment: adults and adolescents over 15 years of age: 2 doses 3 to 4 times daily, for no longer than 3-5 days.

1.5 Pharmaceutical forms: nasal spray.

1.6 Contraindications: hypersensitivity to the active substance or to any of the excipients; history of stroke or risk factors that may lead to stroke; severe or poorly controlled hypertension; severe coronary insufficiency; risk of narrow-angle glaucoma; risk of urinary retention related to urethral-prostatic disorders; history of seizures; in combination with sympathomimetics (oral or nasal use) and with methylphenidate; combination with other decongestants; children under 15 years.

1.7 Relevant warnings: in patients with cardiovascular diseases, and especially in hypertensive patients, the use of nasal decongestants should be subject to medical judgment from time to time. Medicinal products containing tuaminoheptane should be administered with caution in patients with occlusive vascular disease, asthma, diabetes and in therapy with beta-blockers. Medicinal products containing tuaminoheptane should be administered with caution in children and are contraindicated in children under 12 years of age. Prolonged use of preparations containing vasoconstrictors may alter the normal function of the mucous membrane of the nose and sinuses, also inducing drug tolerance. Repeated use for long periods of time can therefore be harmful. Medicinal products containing tuaminoheptane should be used with caution, due to the risk of urinary retention, in the elderly and those patients with prostatic hypertrophy. The use, especially if prolonged, of products for topical use can lead to sensitisation phenomena: in this case it is necessary to stop the treatment and, if necessary, to establish a suitable therapy. In any case, in the absence of a complete therapeutic response within a few days, a doctor should be consulted. The treatment should not be prolonged for more than one week. Medicinal products containing tuaminoheptane can produce positive results in anti-doping tests.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): the following adverse reactions may occur in association with the use of medicinal products containing tuaminoheptane. Their frequency is not known.

Immune system disorders: hypersensitivity.

Psychiatric disorders (especially with prolonged or excessive use): anxiety, hallucinations, delusions.

Nervous system disorders (especially with prolonged or excessive use): headache, restlessness, impatience, insomnia.

Cardiac disorders (especially with prolonged or excessive use): palpitations, tachycardia, arrhythmia.

Vascular disorders: high blood pressure.

Respiratory organs (especially with prolonged or excessive use): dry nose, nasal discomfort, nasal congestion.

GI disorders: nausea.

Skin disorders: hives, rash.

Kidney and urinary tract disorders: urinary retention.

General disorders and application site conditions (especially with prolonged or excessive use): irritability, tolerance.

2.2 Indirect risks (incorrect use): in case of overdose, hypertension, photophobia, intense headache, chest tightness and in children with hypothermia strong sedation may present, which requires the adoption of appropriate emergency measures.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not subject to prescription	In combination with acetylcysteine			
AT	Not authorised				
BE	Not authorised				
BiH	Not authorised				
CH	Not subject to prescription	In combination with acetylcysteine Adults and children > 6 years	1%		
CZ	Not authorised				
DE	Not subject to prescription				
EE	Not authorised				
ES	Not authorised				
FI	Not authorised				
FR	List II	In combination with acetylcysteine	1%		
HR	Not authorised				
HU	Not subject to prescription	In combination with acetylcysteine			
IE	Not authorised				
IT	Not subject to prescription	In combination with acetylcysteine			
LT	Not authorised				
LV	Not authorised				
MK	Not authorised				
NL	Not authorised				
PL	Not authorised				
PT	Not authorised				
RO	Not authorised				
RS	Not subject to prescription	In combination with acetylcysteine Adults and children > 12 years	1%		
SE	Not authorised				
SI	Not authorised				
UK	Not authorised				

No more data available from other member states.

Melclass database[1]: List II + Exemption

3.2 Social dimension of classification:

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

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

Proposed recommendation: tuaminoheptane in combination with acetylcysteine: **Not subject to prescription**.

Criteria: possible self-diagnosis; short-term treatment (no longer than 5 days); systemic effects negligible during short term treatment; not subject to prescription in almost all member states where authorised.

3.2.2 Paediatric use: children > 12 years.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Rhinofluimucil® Résumé des caractéristiques du produit - French National Agency for the Safety of Medicine and Health Products (https://bit.ly/2DlnKbc).

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Cromoglicic Acid

1.2 ATC code: R01AC01

1.3 Therapeutic indications: prophylactic treatment of seasonal (intermittent) and perennial (persistent) allergic rhinitis.

14. Posology and duration of treatment: the dose depends on the severity of the symptoms and exposure to allergens. Usually adults and children > 3 years: 1 dose to each nostril 4-6 times daily. Treatment should be started at least 1 week before allergen exposure.

1.5 Pharmaceutical forms: nasal aerosol: 2% solution (20 mg/mL); MS 2.8 mg/dose; MDD: 22.4 mg; MQP: 300 mg.

1.6 Contraindications: proven allergy against cromoglicic acid.

1.7 Relevant warnings: for topical nasal use only. No interactions with other nasal medicines have been observed.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): transient irritation of the nasal mucosa, congestion and mucosal oedema may occur. Sneezing, rarely bleeding from the nose. There may be wheezing, tightness in the chest, cough, taste disturbances, headache, rash and hypersensitivity reactions, including severe anaphylactic reactions

2.2 Indirect risks (incorrect use): reports of cromoglicic acid poisoning or signs of overdose with this medicine are not known.

2.3 Recent cases at European level: not known.

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	List II	Allergic rhinitis	2.9 mg in each nostril	17 mg in each nostril	NA
BE	Not subject to prescription	Allergic rhinitis	4%	4x daily	15 mL solution
BiH	Not authorised				
CH	Not subject to prescription				
CZ	POM				
DE	Not subject to prescription				
GE	Not subject to prescription				
HR	Not authorised				
IE	Not authorised				
IT	Not subject to prescription				
LT	Not authorised				
MK	Not authorised				
PL	Not subject to prescription	Seasonal and perennial allergic rhinitis	2% = 20 mg/mL 1 nasal dose = 2.8 mg	22.4 mg	300 mg

PT	Not subject to prescription		20 mg/mL		15 mL (300 mg)
RO	List II				
RS	Not authorised				

No more data available from other member states.

Melclass database[1]: Not subject to prescription.

3.2 Social dimension of classification

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

Proposed recommendation: **Not subject to prescription** (adults and children > 3 years; MS: 2.8 mg/dose; MDD: no more than 6 doses daily; MQP: 300 mg).

Criteria: topical mode of action and well-known efficacy, acceptable safety profile, unlikely to cause severe side effects.

3.2.2 Paediatric use: children from 3 years of age.

4. REFERENCES/COMMENTS

4.1 References: SmPC CromoHEXAL 2% nasal aerosol

SmPC Polcrom 2% nasal aerosol

US Food and Drug Administration - Cromolyn sodium nasal solution USP, Nasal spray

Martindale: The Complete Drug Reference – 37th Edition

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Levocabastine

1.2 ATC code: R01AC02

1.3 Therapeutic indications: symptomatic treatment of perennial (persistent) and seasonal (intermittent) allergic rhinitis.

1.4 Posology and duration of treatment: adults: 1 dose to each nostril 2-4 times daily; children > 6 years: 1 dose 2 times daily.

1.5 Pharmaceutical forms: nasal spray, 0.5 mg/mL (0.05%).

1.6 Contraindications: known allergy for levocabastine.

1.7 Relevant warnings: the most common adverse effects reported with levocabastine (nasal use) are headache, nasal irritation, somnolence and fatigue. The use of levocabastine nasal spray is not recommended in those with significant renal impairment. Levocabastine is absorbed after both nasal and ocular use. Systemic availability has been estimated at 60 to 80% after nasal doses. However, absolute peak plasma concentrations are low. Plasma protein binding is about 55%. An elimination half-life of 35 to 40 hours has been reported for all routes of delivery. Elimination of levocabastine is primarily renal with 70% excreted as unchanged drug and 10% as an inactive acetylglucuronide metabolite; the remaining 20% is excreted unchanged in the faeces. Trace amounts of levocabastine have been found in breast milk after ocular and nasal use.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance)

Cardiac disorders - rare: tachycardia

Eye disorders - uncommon: eyelid oedema

GI disorders - common: nausea

General disorders and administrative site conditions - common: fatigue, pain; uncommon: malaise, application site irritation, application site pain, application site dryness; rare: application site burn, application site discomfort

Immune system disorders - uncommon: hypersensitivity

Infections and infestations - common: sinusitis

Nervous system disorders - very common: headache; common: dizziness, somnolence

Respiratory, thoracic and mediastinal disorders - common: pharyngolaryngeal pain, epistaxis, cough; uncommon: dyspnoea, nasal discomfort, nasal congestion, bronchospasm; rare: nasal oedema

2.2 Indirect risks (incorrect use): there have been no reports of overdosing with levocabastine. Some sedation after accidental intake of the contents of the bottle cannot be excluded.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not subject to prescription	Allergic rhinitis	0.1 mg in each nostril	0.4 mg into each nostril	
BE	Not subject to prescription	Fast and lasting relief of symptoms of allergic rhinitis	0.5 mg/mL		
BiH	Not authorised				
CH	Not subject to prescription				
CZ	Not subject to prescription		0.5 mg/mL		10 mL = 5 mg
DE	Not subject to prescription				
GE	Not authorised				
HR	Not authorised				
IE	Not authorised				
IT	Not subject to prescription				
LT	Not authorised				
MK	Not authorised				
PL	Not authorised				
PT	Not authorised				
RO	Not authorised				
RS	Not authorised				
UK	Not authorised				

No more data available from other member states.

Melclass database[1]: Not subject to prescription.

3.2 Social dimension of classification

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

Proposed recommendation: **Not subject to prescription** (treatment of allergic rhinitis; adults and children > 6 years).

Criteria: well-known substance with known safety profile and mild and transient adverse effects.

3.2.2 Paediatric use: children > 6 years 1 dose twice daily.

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference – 37th Edition

SmPC LIVOSTIN 0.5 mg/ml nosní sprej, suspense – available at: Medicinal Products Registry Poland - http://pub.rejestrymedyczne.csioz.gov.pl

Levocabastine Nasal Spray 0.25 mg/mL and 0.5 mg/mL; RMS:DK/H/PSUR/0025/00129.11.2010

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Azelastine

1.2 ATC code: R01AC03

1.3 Therapeutic indications: symptomatic treatment of seasonal (intermittent) allergic rhinitis (e.g. hay fever) and perennial (persistent) allergic rhinitis in patients aged 6 years and over.

1.4 Posology and duration of treatment: adults: one application (0.14 mL) in each nostril twice daily (0.56 mg of azelastine hydrochloride/day). Elderly: there have been no specific studies in the elderly. Children: for children aged 6 years and older, one application (0.14 mL) in each nostril twice daily (0.56 mg of azelastine hydrochloride/day).

This medicine can be used until the symptoms disappear. Azelastine should not be used in children below 6 years of age due to lack of data on safety and efficacy.

1.5 Pharmaceutical forms: nasal spray 0.1%.

1.6 Contraindications: proven allergy against azelastine.

1.7 Relevant warnings: none. To date, no interactions are known for the topical use of azelastine. About 40% of an intranasal dose of azelastine reaches the systemic circulation. Elimination is via hepatic metabolism with excretion mainly in the faeces.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): when given intranasally, irritation of the nasal mucosa and taste disturbances have been reported; somnolence, headache and dry mouth have also been noted in some patients. Taste disturbance can occur after use in the eye.

The following frequencies of undesirable effects were reported:

Common (1-10%): a substance-specific bitter taste may be experienced after administration (often due to incorrect method of application, namely tilting the head too far backwards during administration) which, in rare cases, may lead to nausea.

Uncommon (0.1-1%): a mild, transient irritation of the inflamed nasal mucosa may occur with symptoms such as stinging, itching, sneezing and epistaxis.

In very rare cases (< 0.01%): hypersensitivity reactions (such as rash, pruritus, urticaria) were reported.

Immune system disorders: very rare: hypersensitivity reactions.

Nervous system disorders: common: dysgeusia (unpleasant taste) may be experienced after administration (often due to incorrect method of application, namely tilting the head too far backwards during administration), which may lead to nausea in rare cases. Very rare: dizziness

Respiratory, thoracic and mediastinal disorders: uncommon: nasal discomfort of the inflamed nasal tissue (stinging, itching), sneezing, epistaxis.

GI disorders: rare: nausea.

General disorders: very rare: fatigue (weariness, exhaustion), dizziness or weakness.

Skin and subcutaneous tissue disorders: very rare: rash, pruritus, urticaria.

2.2 Indirect risks (incorrect use): the results of animal studies show that toxic doses can produce CNS symptoms, e.g. excitation, tremor, convulsions. Should these occur in humans, symptomatic and

supportive treatment should be instigated as there is no specific antidote. Gastric lavage is recommended if the overdose is recent. With the nasal route of administration overdosage reactions are not anticipated. There is no experience of the administration of toxic doses of azelastine in humans. Symptoms: in the event of overdose or intoxication, disturbances of the CNS are to be expected based on the results of animal experiments.

2.3 Recent cases at European level: not known.

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not subject to prescription		1 mg/mL		
AT	List II + Exemption		Ex.: nasal application up to 0.1%		
BE	Not subject to prescription	Symptomatic treatment of seasonal allergic rhinitis	1 mg/mL		
BiH	Not subject to prescription	Symptomatic treatment of hay fever (seasonal allergic rhinitis) and non-seasonal (perennial) allergic rhinitis	1.5 mg/mL		45 mg/30 mL
CH	List II + exemption	List II: therapy of seasonal and perennial allergic rhinitis Non-prescription: treatment of seasonal allergic rhinitis (hay fever) in adults and adolescents from 12 years	0.14 mg/application	2 x 2 applications	List II: 10 mg Non-prescription: 5 mg
CZ	POM				
DE	POM + Exemption				
GE	Not subject to prescription				
HR	List I + Exemption	Ex.: symptomatic treatment of seasonal allergic rhinitis and acute exacerbation of perennial rhinitis in adults, adolescents and children above 6 years	Ex.: 1 mg/mL	Ex. 2 x 1 actuation in each nostril	Ex.: 10 mL
IE	List II				
IT	Not subject to prescription				
LT	Not subject to prescription				
MK	Not authorised				
PL	Not subject to prescription	Allergic perennial and seasonal rhinitis Adults and children > 6 years	1 mg/mL	0.56 mg	10 mg
PT	Not subject to prescription	Symptomatic treatment rhinitis allergic symptoms (including symptomatology of hay fever)	1 mg/mL		10 mL (10 mg)
RO	List II				
RS	POM + Exemption	Ex.: treatment of both seasonal (e.g. hay fever) and perennial allergic rhinitis in patients aged 6 years and over	Ex.: 1 mg/mL		Ex.: 10 mL
UK	POM				

No more data available from other member states.

Melclass database[1]: List II + Exemption (exemptions: nasal use; MS: 0.1%).

3.2 Social dimension of classification

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

Proposed recommendation: List II + Exemption

Exemptions: nasal use; treatment of seasonal allergic rhinitis in patients aged 6 years and over; MS: 0.1%; MDD: 0.56 mg; MQP: 10 mg.

Criteria: well-known active substance; known and acceptable safety profile; with the nasal route of administration no overdosage reactions are anticipated.

3.2.2 Paediatric use: children > 6 years.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: SmPC Rhinolast® Nasal Spray C, Jan.2014 available at: https://www.medicines.org.uk/emc/product/1623

SmPC Astelin (azelastine hydrochloride) nasal spray Initial U.S. Approval: 1996, Revised: 10/2014

SmPC ALLERGODIL, 1 mg/mL (0.1%), aerozol do nosa, roztwór, 2013 available at: Medicinal Products Registry Poland - http://pub.rejestrymedyczne.csioz.gov.pl

SmPC Azelastin-POS 1 mg/mL nasal spray, solution; AT/H/0351/002 AT/H/0351/002AT/H/0351, 01.10.2015

Martindale: The Complete Drug Reference – 37th Edition

4.2 Comments: USA Food and Drug Administration: in the treatment of allergic rhinitis in adults and children aged 5 years and over, in the USA, 2 sprays of a similar preparation (supplying 137 micrograms per spray) may be given into each nostril twice daily; children aged 5 years and over may be given 1 spray into each nostril twice daily. In the USA, azelastine is also used in the treatment of non-allergic (vasomotor) rhinitis in adults and children aged 12 years and over. The dose is 2 sprays into each nostril twice daily.

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Antazoline

1.2 ATC code: R01AC04

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Spaglumic Acid

1.2 ATC code: R01AC05

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Thonzylamine

1.2 ATC code: R01AC06

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Nedocromil

1.2 ATC code: R01AC07

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are authorised only in Italy (classification status: not subject to prescription)).

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Olopatadine

1.2 ATC code: R01AC08

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Cromoglicic Acid, Combinations

1.2 ATC code: R01AC51

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing cromoglicic acid in combination with other active substances are authorised only in Italy (classification status: not subject to prescription)).

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, medicines containing cromoglicic acid in combination with other active substances are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Beclometasone

1.2 ATC code: R01AD01

1.3 Therapeutic indications: indicated for the treatment and prevention of allergic rhinitis including hay fever in adults aged 18 years and over.

Category POM: beclometasone is indicated for the treatment and prevention of seasonal and perennial allergic rhinitis, hay fever and vasomotor rhinitis.

Category P: beclometasone is indicated for the treatment of hay fever.

1.4 Posology and duration of treatment:

Category POM: adults and children: there is insufficient clinical data at present to support the recommended use of this drug in children under the age of 6. A dose range of 200 to 400 µg per day is recommended. The recommended dosage for adults and children is 2 sprays into each nostril twice daily. Once control of symptoms has been achieved a single spray into each nostril twice a day may be preferred. However, the minimum dose should be used at which effective control of symptoms is maintained. The total daily dose should not normally exceed 8 sprays (400 micrograms/day). For full therapeutic benefit regular use is essential. Furthermore, it should be explained to the patient that maximum relief may not be obtained with the first few doses and that patient's co-operation to comply with the regular dosage schedule should be sought.

Category P: beclometasone is not recommended for children or adolescents under 18 years of age. A dose range of 200 to 400 µg per day is recommended. Usually a dosing regimen of 2 sprays into each nostril every morning and evening is recommended. The maximum number of sprays that should be administered each day is 8. Once control of symptoms has been achieved a single spray into each nostril twice a day may be preferred. However, the minimum dose should be used at which effective control of symptoms is maintained. If symptoms have not improved within 10 days the doctor should be consulted. This product should not be used continuously for longer than 3 months without consulting your doctor. For full therapeutic benefit regular usage is essential. The co-operation of the patient should be sought to comply with the regular dosage schedule and it should be explained that maximum relief may not be obtained within the first few doses. If a dose is missed, then the next dose should be taken when it is due.

1.5 Pharmaceutical forms: nasal spray suspension: 50 µg/dose and 100 µg/dose.

1.6 Contraindications: haemostasis disorders, including epistaxis. It should not be administered to patients with untreated progressive or latent pulmonary tuberculosis, untreated and unmonitored progressive GI ulcer, infectious rhinitis. Viral, fungal or bacterial infections at the nasal, oral or ocular level that would not be treated specifically also constitute a contraindication.

In addition for category P: the P product should not be used continuously for longer than 3 months without consulting a doctor. Medical advice should be sought before using beclometasone in the case of recent injury or surgery to the nose, or problems with ulceration of the nose.

1.7 Relevant warnings: systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and, more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as CSCR which have been reported after use of systemic and topical corticosteroids.

It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid, if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist. Treatment with higher than recommended doses may result in clinically significant adrenal suppression. If there is evidence for higher than recommended doses being used then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery. Beclometasone will control seasonal allergic rhinitis in most cases. However, an abnormally heavy challenge of summer allergies may, in certain situations, necessitate appropriate additional therapy, especially to control eye symptoms. Asthma is often associated with rhinitis. In this case, the treatment may include an inhaled form topical respiratory and nasal form, both based on corticosteroids. The cumulative doses of these two pathways should be considered because beyond a certain dose there is systemic accumulation and risk of local side effects. It is necessary to remind the patient that this medicine is not indicated for the treatment of the crisis and that a delay of a few days is necessary to evaluate its effects. The administration of doses greater than those recommended is not advisable, given the low efficiency and higher risk of adverse effects (local and systemic). Corticoids may mask some signs of infection, and sometimes a new infection may manifest during their use. In particular, in patients treated with beclometasone, a concomitant bronchopulmonary infection that is bacterial, viral and mycotic may occur. This requires the discontinuation of local corticosteroid treatment and the initiation of appropriate treatment. In case of infections of the nasal passages and paranasal sinuses, appropriate treatment will be established. Nevertheless, these infections do not constitute a specific contraindication to treatment with beclometasone. When glucocorticoid treatment is substituted by the general route with a local glucocorticoid, masked allergy may appear as conjunctivitis, rhinitis and eczema. This allergy can be treated effectively with topical antihistamines or corticosteroids. Caution should also be exercised when replacing oral glucocorticoids with a local glucocorticoid in patients whose adrenocortical function is deficient following treatment with high doses of oral glucocorticoids or after long-term treatment. In these patients, we will monitor regular adrenocortical function, and the dose of glucocorticoids should be carefully reduced. Corticosteroids have a certain antimycotic activity and can, therefore, slow down healing. Caution should also be exercised when there is a history of nasal septal ulcer, nasal surgery, trauma or recurrent epistaxis.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (Pharmacovigilance): systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. Systemic effects include hypothalamo-pituitary-adrenal (HPA) axis suppression and growth retardation in children and adolescents. Rare cases of nasal septal perforation have been reported following the use of intranasal corticosteroids. Rare cases of raised intraocular pressure, cataract or glaucoma have been reported. Blurred vision may be reported with unknown frequency.

2.2 Indirect risks (incorrect use): overdose may result in inhibition of HPA-axis and then signs of hypercorticism such as weight gain, hypertension, acneiform lesions, Cushingoid signs. The patient will be considered steroid-dependent and will be treated with an adequate maintenance dose of systemic corticosteroid such as prednisolone. As soon as the situation is stabilised, treatment with beclometasone may be reinstated. The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of the HPA-axis. No special emergency action need be taken. Treatment with beclometasone should be continued at the recommended dose. HPA function reverses in 1 or 2 days.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not authorised				
BE	POM	Basic treatment of seasonal allergic rhinitis			
BiH	Not authorised				
CH	Not subject to prescription	Therapy of seasonal allergic rhinitis (hay fever) in adults over 18 years of age.	50 mcg	20 mcg	5000 mcg
DE	POM + Exemption	Ex.: seasonal allergic rhinitis; adults only; prior physician's diagnosis needed		Ex.: 400 mcg	
GE	Not subject to prescription				
HR	Not authorised				
IE	List II				
LT	Not authorised				
MK	Not authorised				
PL	POM				
PT	Not subject to prescription	Prevention and treatment of perennial and seasonal allergic rhinitis with medical diagnosis in patients over 18 years of age.	50 mcg/dose		
RO	List I	Prophylaxis and treatment of seasonal, perennial and vasomotor rhinitis.	100 mcg/dose	200 mcg/dose	30 mL
RS	POM				
UK	POM + Exemption	Ex.: adults only; no more than 7 days	Ex.: 50 mcg	Ex.: 400 mcg	

No more data available from other member states.

Melclass database[1]: -

3.2 Social dimension of classification:

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

Proposed recommendation: **List I + Exemption**

Exemptions: nasal use; seasonal allergic rhinitis; adults only; MS: 50 mcg; MDD: 400 mcg.

Criteria: under the exemptions stated, the use of the product is considered to be safe; well-known use; self-assessment possible.

3.2.2 Paediatric use: there is insufficient clinical data at present to support the recommended use of this drug in children under the age of 6. It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid, if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

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

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Prednisolone

1.2 ATC code: R01AD02

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Dexamethasone

1.2 ATC code: R01AD03

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Flunisolide

1.2 ATC code: R01AD04

1.3 Therapeutic indications: perennial allergic rhinitis; seasonal allergic rhinitis, especially hay fever.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Budesonide

1.2 ATC code: R01AD05

1.3 Therapeutic indications: prevention and treatment of seasonal allergic rhinitis (hay fever).

1.4 Posology and duration of treatment: rhinitis (adults including the elderly): recommended to start with 256 mcg/day. Once daily dosing: 2 applications of 64 mcg into each nostril each morning. Twice daily dosing: one application of 64 mcg into each nostril morning and evening. The minimum dose should be used at which effective control of symptoms is maintained. The patient should be informed that the full effect of budesonide is not achieved until after a few days' treatment. Treatment of seasonal rhinitis should, if possible, start before exposure to the allergens. If symptoms are not controlled, or persist for longer than 2 weeks of treatment, medical advice must be sought. Concomitant treatment may sometimes be necessary to counteract eye symptoms caused by the allergy. Budesonide should not be used continuously for longer than 3 months without consulting your doctor or pharmacist. Patients should be reminded of the importance of taking this medicine regularly. The dose should be titrated to the lowest dose at which effective control of symptoms is achieved.

Paediatric population: this spray should not be used in children and adolescents under 18 years of age. There is insufficient data to recommend the use of budesonide in children.

1.5 Pharmaceutical forms: nasal spray: 32 mcg/dose; 64 mcg/dose; 100 mcg/dose.

1.6 Contraindications: not to be used in patients with untreated progressive or latent pulmonary tuberculosis, untreated and unmonitored progressive GI ulcer, infectious rhinitis. Viral, fungal or bacterial infections at the nasal, oral or ocular level that would not be treated specifically also constitute a contraindication.

1.7 Relevant warnings: this medicine should not be used for more than 3 months continuously without consulting a doctor or pharmacist. Special care is demanded in treatment of patients transferred from oral steroids to this medicine where disturbances of the HPA-axis could be expected. Special care is needed in patients with fungal and viral infections of the airways and in patients with active or quiescent pulmonary tuberculosis. Special care is needed where there is an infection in the nasal passages or sinuses, or in the case of recent surgery to the nose, or problems with ulceration in the nose. Concomitant treatment of seasonal rhinitis may sometimes be necessary to counteract eye symptoms caused by the allergy. Reduced liver function affects the elimination of corticosteroids, causing lower elimination rate and higher systemic exposure. Be aware of possible systemic side effects. Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as CSCR which have been reported after use of systemic and topical corticosteroids.

Paediatric population: the long-term effects of nasal glucocorticosteroids in children are not fully known. Physicians should closely follow the growth of children taking glucocorticosteroids for longer term by any route, and weigh the benefits of the glucocorticosteroid therapy against the possibility of growth suppression.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (Pharmacovigilance): in rare cases, signs or symptoms of systemic glucocorticosteroid-side effects such as Cushing's syndrome, Cushingoid features, psychomotor hyperactivity, sleep

disorders, anxiety, depression or aggression (particularly in children) may occur with nasal glucocorticosteroids, probably depending on dose, exposure time, concomitant and previous corticosteroid exposure, and individual sensitivity. In paediatric population growth retardation has been reported in children receiving intranasal steroids. Therefore, due to the risk of growth retardation in the paediatric population, growth should be monitored.

2.2 Indirect risks (incorrect use): acute overdose with this medicine, even in excessive doses, is not expected to be a clinical problem. Inhalation of high doses of corticosteroids may lead to suppression of the HPA-axis function.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	List I	Rhinitis, treatment of nasal polyp	256 mcg	256 mcg	N.A.
BE	POM	Basic treatment of attacks of seasonal or chronic allergic rhinitis and idiopathic rhinitis	100 mcg/dose (inhaler)		
BiH	POM	Allergic rhinitis, non-allergic rhinitis and nasal polyps	50 mcg/dose		200 doses
CH	List II				
DE	POM				
GE	POM				
HR	List II	Seasonal and perennial allergic rhinitis and vasomotor rhinitis. Treatment of nasal polyps.	50 mcg/actuation	400 mcg	10 mL
IE	Not authorised				
IT	List II				
LT	Not authorised				
MK	Not subject to prescription	Seasonal allergic rhinitis, non-allergic rhinitis, nasal polyps	50 mcg/dose	400 mcg	200 doses
PL	POM				
PT	POM + Exemption	Pharmacy only: prevention and treatment of seasonal allergic rhinitis, and perennial allergic or non-allergic rhinitis for adults. Prescription only: symptomatic treatment of allergic rhinitis (seasonal and chronic) and vasomotor rhinitis, as well as treatment of nasal polyposis and prophylaxis of recurrent polyps after polypectomy. Adults and children over 6 years old.	Pharmacy-only medicine (64 mcg/dose) Prescription-only medicine (100 mcg/dose)		
RO	List I	Allergic and non-allergic rhinitis and perennial rhinitis. Symptomatic and prophylactic treatment of adenoid vegetation.	32 mcg/dose	256 mcg	120 doses
RS	Not authorised				

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

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

Proposed recommendation: **List I**

Criteria: short-term use and medical supervision required.

3.2.2 Paediatric use: growth retardation has been reported in children receiving intranasal steroids. Due to the risk of growth retardation in the paediatric population, growth should be monitored.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Betamethasone

1.2 ATC code: R01AD06

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Tixocortol

1.2 ATC code: R01AD07

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluticasone

1.2 ATC code: R01AD08

1.3 Therapeutic indications: indicated for the prophylaxis and treatment of allergic rhinitis including hay fever and that caused by other airborne allergens such as house dust mites and animal dander. It provides symptomatic relief of sneezing, itchy and runny nose, itchy and watery eyes, nasal congestion and associated sinus discomfort.

1.4 Posology and duration of treatment:

50 micrograms/spray: adults aged 18 years and over: for the prophylaxis and treatment of allergic rhinitis: 2 sprays into each nostril once a day (200 mcg), preferably in the morning, is recommended. In some cases 2 sprays into each nostril twice a day (400 mcg) may be required. Once symptoms are under control a maintenance dose of one spray per nostril once a day (100 mcg) may be used. If symptoms recur the dosage may be increased accordingly. The maximum daily dose should not exceed 4 sprays into each nostril (400 mcg). The minimum dose at which the effective control of symptoms is maintained should be used. The maximum daily dose should not exceed 4 sprays into each nostril. The duration of treatment should be restricted to the period that corresponds to allergenic exposure. Prophylaxis of allergic rhinitis requires treatment before contact with allergen. For full therapeutic benefit regular usage is recommended. Maximum benefit may require 3-4 days of continuous treatment in some people.

Elderly patients: the normal adult dosage is applicable.

Children and adolescents under 18 years of age: should not be used by children and adolescents under 18 years of age.

27.5 micrograms/spray: adults and adolescents (12 years and over): the recommended starting dose is 2 spray actuations (27.5 micrograms of fluticasone per spray actuation) in each nostril once daily (total daily dose: 110 micrograms). Once adequate control of symptoms is achieved, dose reduction to one spray actuation in each nostril (total daily dose 55 micrograms) may be effective for maintenance. The dose should be titrated to the lowest dose at which effective control of symptoms is maintained.

Children (6 to 11 years of age): the recommended starting dose is one spray actuation (27.5 micrograms of fluticasone per spray actuation) in each nostril once daily (total daily dose, 55 micrograms).

Patients not adequately responding to one spray actuation in each nostril once daily (total daily dose, 55 micrograms) may use 2 spray actuations in each nostril once daily (total daily dose, 110 micrograms). Once adequate control of symptoms is achieved, dose reduction to one spray actuation in each nostril once daily (total daily dose, 55 micrograms) is recommended. For full therapeutic benefit regular, scheduled usage is recommended. Onset of action has been observed as early as 8 hours after initial administration. However, it may take several days of treatment to achieve maximum benefit, and the patient should be informed that their symptoms will improve with continuous regular use.

Children under 6 years of age: the safety and efficacy of fluticasone in children under the age of 6 years has not been established.

1.5 Pharmaceutical forms: nasal Spray: 27.5 and 50 micrograms/spray

1.6 Contraindications: epistaxis; viral or fungal infections or major local infections.

1.7 Relevant warnings: treatment should be stopped or the advice of a doctor sought if an improvement is not seen within 7 days. The advice of a doctor or pharmacist should also be sought if symptoms have improved but are not adequately controlled.

The medication should not be used for more than 3 months continuously without consulting a doctor. Medical advice should be sought before using in the following cases: concomitant use of other corticosteroid products, such as tablets, creams, ointments, asthma medications, similar nasal sprays or eye/nose drops; an infection in the nasal passages or sinuses; recent injury or surgery to the nose, or problems with ulceration in the nose. In most cases it will control seasonal allergic rhinitis; however in the event of an abnormally heavy challenge of summer allergens appropriate additional therapy may be necessitated in certain instances. Such an instance may particularly be to control eye symptoms.

Systemic corticosteroid effects: systemic effects of nasal corticosteroid may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Treatment with higher than recommended doses of nasal corticosteroids may result in clinically significant adrenal suppression. If there is evidence for higher than recommended doses being used, then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery. Fluticasone 110 micrograms once daily was not associated with HPA-axis suppression in adult, adolescent or paediatric subjects. However the dose of intranasal fluticasone should be reduced to the lowest dose at which effective control of the symptoms of rhinitis is maintained. As with all intranasal corticosteroids, the total systemic burden of corticosteroids should be considered whenever other forms of corticosteroid treatment are prescribed concurrently. If there is any reason to believe that adrenal function is impaired, care must be taken when transferring patients from systemic steroid treatment to fluticasone.

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

Adrenal suppression may occur to clinically significant levels as a result of treatment with higher than recommended doses of nasal corticosteroids. If there is evidence for higher than recommended doses being used then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

Incidences of significant interactions between fluticasone and potent inhibitors of the cytochrome P450 3A4 system (e.g. ketoconazole and protease inhibitors such as ritonavir) may occur. This may result in increased systemic exposure to fluticasone (e.g. Cushing's syndrome and adrenal suppression have been observed). Therefore concomitant use of fluticasone and cytochrome P450 3A4 inhibitors should be avoided unless the expected benefit exceeds the possible risk of systemic adverse reaction of corticosteroids.

In patients who have tuberculosis, any type of untreated infection, ocular herpes or have had a recent surgical operation or injury to the nose or mouth, the possible benefits of the treatment should be weighed against possible hazards.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (Pharmacovigilance): the following convention has been used for the classification of frequencies: very common ≥1/10; common ≥1/100 to <1/10; uncommon ≥1/1000 to <1/100; rare ≥1/10,000 to <1/1000; very rare <1/10,000. An overview of the adverse reactions reported with fluticasone is reported in the table below:

Immune system disorders	
Rare	Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria.
Nervous system disorders	
Common	Headache.
Eye disorders	

Not known	Transient ocular changes, vision blurred
Respiratory, thoracic and mediastinal disorders	
Very common	Epistaxis
Common	Nasal ulceration
Uncommon	Rhinalgia, nasal discomfort (including nasal burning, nasal irritation, and nasal soreness), nasal dryness.
Very rare	Nasal septum perforation
Musculoskeletal and connective tissue disorders (Children)	
Not known	Growth retardation

2.2 Indirect risks (incorrect use): administration of doses higher than those recommended over a long period of time may lead to temporary suppression of adrenal function. There is no data available on the effects of acute or chronic overdosage with fluticasone. Intranasal administration of fluticasone propionate at 20 times the recommended dose in adults (2 mg twice daily) for 7 days to healthy human volunteers had no effect on hypothalamo-pituitary-adrenal axis function.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	List I	Allergic rhinitis, nasal polyp	400 mcg into each nostril	400 mcg into each nostril	N.A.
BE	POM + Exemption	Ex.: symptomatic treatment of allergic rhinitis	Ex.: 50 mcg	Ex.: 200 mcg	
BiH	Not subject to prescription	Allergic rhinitis including hay fever, symptomatic relief of sneezing, itchy and runny nose, itchy and watery eyes, nasal congestion and associated sinus discomfort	50 mcg/dose		60 doses
CH	List II				
DE	POM + Exemption	Ex.: symptomatic treatment of allergic rhinitis			
GE	Not subject to prescription				
HR	List II	The prophylaxis and treatment of seasonal allergic rhinitis (including hay fever) and perennial rhinitis.	50 mcg/dose	4 sprays into each nostril	120 doses
IE	List II				
IT	List II				
LT	POM + Exemption	Ex.: symptomatic treatment of allergic rhinitis due to hay fever or other airborne allergens (such as dust mites, mould spores, or animal dander).	Ex.: 50 mcg/dose	Ex.: 200 mcg	Ex.: 60 sprays per bottle
MK	POM		50 mcg/dose		120 doses
PL	POM				
PT	Not subject to prescription (P)		50 mcg/dose	200 mcg	
RO	List I	Indicated in the symptomatic treatment of nasal polyps, prophylaxis and treatment of seasonal allergic rhinitis (including hay fever) and the like, perennial rhinitis.	50 mcg/dose	200 mcg	120 dose
RS	POM + Exemption	Ex.: prophylaxis and	Ex.: 50 mcg/dose	Ex.: 200 mcg	Ex.: 60 doses

		treatment of allergic rhinitis including hay fever and that caused by other airborne allergens.			per pack

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

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

Proposed recommendation: **List I + Exemption**

Exemptions: nasal use; MS: 50 mcg/dose; MDD: 200 mcg; MQP: 60 doses; seasonal allergic rhinitis; adults only.

Criteria: under the exemptions stated, the use of the product is considered to be safe; known use; self-assessment possible; medical advice to be sought after 3 days of use if symptoms do not improve or worsen.

3.2.2 Paediatric use: growth retardation: growth retardation has been reported in children receiving nasal corticosteroids at licensed doses. A reduction in growth velocity has been observed in children treated with fluticasone 110 micrograms daily for one year. Therefore, children should be maintained on the lowest possible efficacious dose which delivers adequate symptom control. In addition, the safety in children under 6 years has not been well established. Frequency, type and severity of adverse reactions observed in the paediatric population are similar to those in the adult population.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Mometasone

1.2 ATC code: R01AD09

1.3 Therapeutic indications: mometasone is indicated for use in adults and children 6 years of age and older to treat the symptoms of seasonal allergic or perennial allergic rhinitis. In patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis, prophylactic treatment with mometasone may be initiated up to 4 weeks prior to the anticipated start of the pollen season. Mometasone is indicated for the symptomatic treatment of nasal polyps in adults 18 years of age and older.

1.4 Posology and duration of treatment: seasonal or perennial allergic rhinitis: the usual recommended dose is 2 actuations (50 micrograms/actuation) in each nostril once daily (total dose 200 micrograms). Once symptoms are controlled, dose reduction to one actuation in each nostril (total dose 100 micrograms) may be effective for maintenance. If symptoms are inadequately controlled, the dose may be increased to a maximum daily dose of 4 actuations in each nostril once daily (total dose 400 micrograms). Dose reduction is recommended following control of symptoms. Mometasone demonstrated a clinically significant onset of action within 12 hours after the first dose in some patients with seasonal allergic rhinitis; however, full benefit of treatment may not be achieved in the first 48 hours. Therefore, the patient should continue regular use to achieve full therapeutic benefit.

Paediatric population: children between the ages of 6 and 11 years: the usual recommended dose is one actuation (50 micrograms/actuation) in each nostril once daily (total dose 100 micrograms). Mometasone should not be used in children below age of 6 years because of insufficient data on safety and efficacy.

Nasal polyposis: the usual recommended starting dose for polyposis is 2 actuations (50 micrograms/actuation) in each nostril once daily (total daily dose of 200 micrograms). If after 5 to 6 weeks symptoms are inadequately controlled, the dose may be increased to a daily dose of 2 sprays in each nostril twice daily (total daily dose of 400 micrograms). After effective control of symptoms is maintained, the dose should be lowered to once daily. If no improvement in symptoms is seen after 5 to 6 weeks of twice daily administration, alternative therapies should be considered. Efficacy and safety studies of mometasone for the treatment of nasal polyposis were 4 months in duration.

Paediatric population: it should not be used in children below age of 18 years because of insufficient data on safety and efficacy.

1.5 Pharmaceutical forms: nasal spray 50 mcg/dose.

1.6 Contraindications: presence of untreated localised infection involving the nasal mucosa. Patients who have experienced recent nasal surgery or trauma until healing has occurred.

1.7 Relevant warnings: patients using mometasone over long-term periods should be examined periodically for possible changes in the nasal mucosa. If localised fungal infection of the nose or pharynx develops, discontinuance of mometasone therapy or appropriate treatment may be required. Persistence of nasopharyngeal irritation may be an indication for discontinuing mometasone. Patients who are transferred from long-term administration of systemically active corticosteroids to mometasone require careful attention. Systemic corticosteroid withdrawal in such patients may result in adrenal insufficiency for a number of months until recovery of HPA-axis function. Such transfer may also unmask pre-existing allergic conditions, such as allergic conjunctivitis and eczema, previously suppressed by systemic corticosteroid therapy. The safety and efficacy of mometasone has not been studied for use in the treatment of unilateral polyps, polyps associated with cystic fibrosis or polyps that completely obstruct the nasal cavities. Unilateral polyps that are unusual or irregular in appearance, especially if ulcerating or bleeding, should be further evaluated. Patients receiving corticosteroids who are potentially immunosuppressed should be warned of the risk of exposure to certain infections (e.g. chickenpox, measles) and of the importance of obtaining medical advice if such exposure occurs. Following the use of intranasal corticosteroids, instances of nasal septum perforation or increased intraocular pressure have been reported very rarely.

Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

Paediatric population: systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses. It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid, if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (Pharmacovigilance): epistaxis was generally self-limiting and mild in severity, and occurred at a higher incidence compared to placebo (5%), but at a comparable or lower incidence when compared to the active control nasal corticosteroids studied (up to 15%) as reported in clinical studies for allergic rhinitis. The incidence of all other adverse events was comparable with that of placebo. In patients treated for nasal polyposis, the overall incidence of adverse events was similar to that observed for patients with allergic rhinitis. Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.

Treatment-related adverse reactions (≥1%) reported in clinical trials in patients with allergic rhinitis or nasal polyposis and post-marketing regardless of indication are presented below. Frequencies are defined as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100). The frequency of post-marketing adverse events are considered as "not known".

Treatment-related adverse reactions			
	Very common	**Common**	**Not known**
Infections and infestations		Pharyngitis Upper respiratory tract infection†	
Immune system disorders			Hypersensitivity including anaphylactic reactions, angioedema, bronchospasm, and dyspnoea
Nervous system disorders		Headache	
Eye disorders			Glaucoma Increased intraocular pressure Cataracts Vision blurred Central serous chorioretinopathy (CSCR)
Respiratory, thoracic and mediastinal disorders	Epistaxis	Epistaxis Nasal burning Nasal irritation Nasal ulceration	Nasal septum perforation
GI disorders		Throat irritation*	Disturbances of taste and smell

2.2 Indirect risks (incorrect use): symptoms: inhalation or oral administration of excessive doses of corticosteroids may lead to suppression of HPA-axis function. Management: because the systemic bioavailability of mometasone is <1%, overdose is unlikely to require any therapy other than observation, followed by initiation of the appropriate prescribed dosage.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	POM		50 mcg/dose	400 mcg	18 g
AT	List I	Allergic rhinitis, nasal polyp	100 mcg into each nostril	800 mcg into each nostril	N.A.
BE	POM + Exemption	Ex.: Symptomatic treatment of allergic rhinitis	Ex.: mcg/dose	Ex.: 200 mcg	
BiH	POM	Seasonal allergic or perennial rhinitis, nasal polyps in adults 18 years of age and older	50 mcg/dose		140 doses
CH	List II + Exemption	Ex.: intended for use in adults for symptomatic treatment of seasonal allergic rhinitis, provided the initial diagnosis of seasonal allergic rhinitis has been made by a doctor.	Ex.: mcg/dose	Ex.: 200 mcg	Ex.: 3000 mcg
DE	POM + Exemption	Ex.: intended for use in adults for symptomatic treatment of seasonal allergic rhinitis,			
GE	Not subject to prescription				
HR	List II	Treatment of symptoms of seasonal allergic or perennial rhinitis (in adults and children 3 years of age and older). Treatment of nasal polyps in adults.	50 mcg/dose	4 sprays into each nostril	3 x 140 doses
IE	List I				
IT	List II				
LT	POM				
MK	POM		50 mcg/dose	200 mcg	140 doses
PL	POM				
PT	POM				
RO	List I				
RS	POM				
SE	POM + Exemption		Ex.: 50 mcg/dose		Ex.: 140 doses
UK	POM + Exemption	Ex.: nasal use	Ex.: 50 mcg/dose		

No more data available from other member states.

Melclass database[1]: List I

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

3.2 Social dimension of classification:

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

Proposed recommendation: **List I + Exemption**

Exemptions: nasal use; MS: 50 mcg/dose; MDD: 200 mcg; MQP: 60 doses; seasonal allergic rhinitis; adults only.

Criteria: under the exemptions stated, the use of the product is considered to be safe; known use; self-assessment possible; medical advice to be sought after 3 days of use if symptoms do not improve or worsen.

3.2.2 Paediatric use: systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses. It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Triamcinolone

1.2 ATC code: R01AD11

1.3 Therapeutic indications: indicated for the treatment of symptoms of seasonal and perennial allergic rhinitis.

1.4 Posology and duration of treatment: patients aged 12 years and over: the recommended starting dose is 220 micrograms as 2 sprays in each nostril once daily. Once symptoms are controlled patients can be maintained on 110 micrograms (1 spray in each nostril once daily).

Paediatric patients aged 6 to 12 years: the recommended dose is 110 micrograms as 1 spray in each nostril once daily. In patients with more severe symptoms, a dose of 220 micrograms may be used. However, once symptoms are controlled, patients should be maintained on the lowest effective dose.

Paediatric population: until further evidence is available, continuous use beyond 3 months in children under 12 years is not recommended.

1.5 Pharmaceutical forms: nasal spray and suspension - 55 micrograms/dose.

1.6 Contraindications: presence of untreated localised infection involving the nasal mucosa.

1.7 Relevant warnings: if there is any reason to suppose that adrenal function is impaired, care must be taken while transferring patients from systemic steroid treatment to triamcinolone. In clinical studies with triamcinolone administered intranasally, the development of localised infections of the nose and pharynx with *Candida albicans* has rarely occurred. When such an infection develops it may require treatment with appropriate local therapy and temporary discontinuation of treatment with triamcinolone. Because of the inhibitory effect of corticosteroids on wound healing in patients who have experienced recent nasal septal ulcers, nasal surgery or trauma, triamcinolone should be used with caution until healing has occurred. Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Treatment with higher than recommended doses may result in clinically significant adrenal suppression. If there is evidence of using higher than recommended doses then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery. Glaucoma and/or cataracts have been reported in patients receiving nasal corticosteroids. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma and/or cataracts. Visual disturbance may also be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as CSCR, which have been reported after use of systemic and topical corticosteroids.

Paediatric population: as experience with triamcinolone in children under 6 years of age is limited, use in this age group is not recommended. Reduction in growth velocity has been reported in children receiving nasal corticosteroids, including triamcinolone at licensed doses. It is recommended that the height of children receiving treatment with nasal corticosteroids is regularly monitored. Therapy should be managed with the aim of reducing the dose of nasal corticosteroid, if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist. The long-term effects of reduction in growth velocity associated with nasal corticosteroids, including the impact on final adult height are unknown.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (Pharmacovigilance): Immune system disorders: hypersensitivity (including rash, urticaria, pruritus and facial oedema).

Psychiatric disorders: insomnia.

Nervous system disorders: headache, dizziness, alterations of taste and smell.

Eye disorders: cataract, glaucoma, increased ocular pressure, blurred vision.

Respiratory, thoracic and mediastinal disorders: bronchitis, epistaxis, cough, nasal septum perforations, nasal irritation, dry mucous membrane, nasal congestion, sneezing, dyspnoea.

GI disorders: dyspepsia, tooth disorder, nausea.

General disorders and administration site conditions: fatigue.

Investigations: decreased blood cortisol.

Reduction of growth velocity has been observed in children during a post-marketing clinical trial with triamcinolone.

Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. Growth retardation has been reported in children receiving intranasal steroids.

2.2 Indirect risks (incorrect use): like any other nasally administered corticosteroid, acute overdosing with triamcinolone is unlikely in view of the total amount of active ingredient present. In the event that the entire contents of the bottle were administered all at once, via either oral or nasal application, clinically significant systemic adverse events would most likely not result. The patient may experience some GI upset if taken orally.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not authorised				
BE	POM + Exemption	Ex.: symptomatic treatment of allergic rhinitis. 18 years and older	Ex.: 50 mcg	Ex.: 200 mcg	
BiH	Not authorised				
CH	List II + Exemption	Ex.: treatment of seasonal rhinitis including hay fever in adults.	Ex.: 55 mcg	Ex.: 220 mcg	Ex.: 1650 mcg
DE	POM				
GE	Not subject to prescription				
HR	List II	Treatment of symptoms of seasonal allergic or perennial rhinitis (in adults and children 6 years of age and older).	5 mcg/dose	220 mcg	120 doses
IE	Not subject to prescription (P)	Indicated for the treatment of symptoms of seasonal allergic rhinitis. Without medical supervision, the product is not recommended for use longer than 3 months. Adults (18 and over) only	55 mcg/dose	The recommended starting dose is 220 mcg as 2 sprays in each nostril once	20 mL
IT	List II				

LT	POM				
MK	Not authorised				
PL	POM				
PT	POM				
RO	List II				
RS	Not authorised				
SE	POM + Exemption		Ex.: 55 mcg/dose		Ex.: 120 doses

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

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

Proposed recommendation: **List I + Exemption**

Exemptions: nasal use; MS: 50 mcg; MDD: 200 mcg; MQP: 30 doses; adults only; seasonal allergic rhinitis.

Criteria: under the exemptions stated, the use of the product is considered to be safe; known use; self-assessment possible; medical advice to be sought after 3 days of use if symptoms do not improve or worsen.

3.2.2 Paediatric use: reduction of growth velocity has been observed in children during a post-marketing clinical trial with triamcinolone. Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. Growth retardation has been reported in children receiving intranasal steroids.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

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

4.2 Comments: note: 55 mcg triamcinolone acetonide is equivalent to 50 mcg of triamcinolone.

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluticasone Furoate

1.2 ATC code: R01AD12

1.3 Therapeutic indications: for the treatment of allergic rhinitis.

1.4 Posology and duration of treatment: adults and adolescents (12 years and over): the recommended starting dose is 2 spray actuations (27.5 micrograms of fluticasone furoate per spray actuation) in each nostril once daily (total daily dose: 110 micrograms). Once adequate control of symptoms is achieved, dose reduction to one spray actuation in each nostril (total daily dose: 55 micrograms) may be effective for maintenance. The dose should be titrated to the lowest dose at which effective control of symptoms is maintained.

Children (6 to 11 years of age): the recommended starting dose is one spray actuation (27.5 micrograms of fluticasone furoate per spray actuation) in each nostril once daily (total daily dose: 55 micrograms).

Patients not adequately responding to one spray actuation in each nostril once daily (total daily dose, 55 micrograms) may use 2 spray actuations in each nostril once daily (total daily dose, 110 micrograms). Once adequate control of symptoms is achieved, dose reduction to one spray actuation in each nostril once daily (total daily dose, 55 micrograms) is recommended. For full therapeutic benefit regular, scheduled usage is recommended. Onset of action has been observed as early as 8 hours after initial administration. However, it may take several days of treatment to achieve maximum benefit, and the patient should be informed that their symptoms will improve with continuous regular use. The duration of treatment should be restricted to the period that corresponds to allergenic exposure.

Children under 6 years of age: the safety and efficacy of fluticasone furoate in children under the age of 6 years has not been established.

Elderly patients, renal impairment and hepatic impairment: no dose adjustment is required in these populations.

1.5 Pharmaceutical forms: nasal spray: 27.5 mcg/dose.

1.6 Contraindications: fluticasone furoate should not be administered to patients with untreated progressive or latent pulmonary tuberculosis, untreated and unmonitored progressive GI ulcer, and infectious rhinitis. In addition, viral, fungal or bacterial infections at the nasal, oral or ocular level that would not be treated specifically also constitute a contraindication.

1.7 Relevant warnings: systemic effects of nasal corticosteroid may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Treatment with higher than recommended doses of nasal corticosteroids may result in clinically significant adrenal suppression. If there is evidence for higher than recommended doses being used, then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery. Fluticasone furoate once daily was not associated with HPA-axis suppression in adult, adolescent or paediatric subjects. However the dose of intranasal fluticasone furoate should be reduced to the lowest dose at which effective control of the symptoms of rhinitis is maintained. As with all intranasal corticosteroids, the total systemic burden of corticosteroids should be considered whenever other forms of corticosteroid treatment are prescribed concurrently. If there is any reason to believe that adrenal function is impaired, care must be taken when transferring patients from systemic steroid treatment to fluticasone furoate. Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as CSCR which have been reported after use of systemic and topical corticosteroids. Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses. A reduction in growth velocity has been observed in children treated with fluticasone

furoate daily for one year. Therefore, children should be maintained on the lowest possible efficacious dose which delivers adequate symptom control. It is recommended that the growth of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist. Concomitant administration with ritonavir is not recommended because of the risk of increased systemic exposure of fluticasone furoate.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (Pharmacovigilance): the most commonly reported adverse reactions during treatment with fluticasone furoate are epistaxis, nasal ulceration and headache. The most serious undesirable effects are rare reports of hypersensitivity reactions, including anaphylaxis (less than 1 case per 1000 patients).

Selected adverse reactions: epistaxis: epistaxis was generally mild to moderate in intensity. In adults and adolescents, the incidence of epistaxis was higher in longer-term use (more than 6 weeks) than in short-term use (up to 6 weeks).

Systemic effects: systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.

Growth retardation has been reported in children receiving nasal corticosteroids. In a one-year clinical study assessing growth in pre-pubescent children receiving 110 micrograms of fluticasone furoate once daily, an average treatment difference of -0.27 cm per year in growth velocity was observed compared to placebo

Paediatric population: the safety in children under 6 years has not been well established. Frequency, type and severity of adverse reactions observed in the paediatric population are similar to those in the adult population. Epistaxis: in paediatric clinical studies of up to 12 weeks duration the incidence of epistaxis was similar between patients receiving fluticasone furoate and patients receiving placebo.

2.2 Indirect risks (incorrect use): in a bioavailability study, intranasal doses of up to 2640 micrograms per day were administered over 3 days with no adverse systemic reactions observed. Acute overdose is unlikely to require any therapy other than observation.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	POM		27.5 mcg/dose	110 mcg	120 doses
AT	List I				
BE	Not subject to prescription	Adults (18 years and older). Symptomatic treatment of allergic rhinitis.	50 mcg	200 mcg/dose	
BiH	POM	Allergic rhinitis	27.5 mcg/dose	110 mcg	3300 mcg
CH	List II				
DE	POM				
EE	POM				
FR	List i				

GE	Not subject to prescription				
HR	List II	Treatment of symptoms of allergic rhinitis (in adults and children 6 years of age and older).	27.5 mcg/spray	110 mcg (adults), 55 mcg (children)	120 sprays
IE	List II				
IT	List II				
LT	POM				
MK	POM		27.5 mcg/dose	110 mcg	120 doses
NL	POM				
PL	POM				
PT	POM				
RO	List I				
RS	POM				

No more data available from other member states.

Melclass database[1]: POM

3.2 Social dimension of classification:

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

Proposed recommendation: **List I**

Criteria: short-term use and medical supervision required.

3.2.2 Paediatric use: not recommended in children under 6 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference and website of the EMA (https://www.ema.europa.eu/en).

4.2 Comments: medicinal products containing fluticasone furoate have been authorised through the centralised procedure.

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Ciclesonide

1.2 ATC code: R01AD13

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Prednisolone, Combinations

1.2 ATC code: R01AD52

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing prednisolone in combination with other active substances are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Dexamethasone, Combinations

1.2 ATC code: R01AD53

1.3 Therapeutic indications: short symptomatic treatment of inflammatory rhinitis (allergic rhinitis).

1.4 Posology and duration of treatment: it should be used in moderation because of its long-lasting and profound effect. It is advised to perform 1 spray into each nostril 2 to 3 times a day. The administration can be repeated up to 6 intakes per 24 hours for adults. Children may not use more than 4 sprays per 24 hours (7 to 9 years), 5 sprays per 24 hours (10 to 12 years) or 6 sprays per 24 hours (from 13 years). It is only suitable for adults and children from 6 years. It is necessary to administer the lowest effective dose with relief obtained. The treatment should not take longer than 5 days.

1.5 Pharmaceutical forms: nasal spray containing dexamethasone 0.02 mg and tramazoline hydrochloride 0.12 mg.

1.6 Contraindications: contraindicated in the following cases: hypersensitivity to the active substances or to any excipients; mycotic nasal infections, tuberculosis, viral diseases (herpes, chicken pox, etc.); infections of the nose, mouth, eyes and/or upper respiratory tract because of the corticoid component; children under 7 years of age; treatment with MAOIs; dry rhinitis; glaucoma, including closed-chamber angle glaucoma (theoretically possible interaction with the sympathicomimetic component); pregnancy and breastfeeding; after cranial surgery through the nose.

1.7 Relevant warnings: the prolonged administration of vasoconstrictors is not recommended as it may result in chronic inflammation (and therefore nasal congestion) and atrophy of the mucosa. Prolonged use of corticoids in doses higher than those recommended may lead to symptoms of hypercorticism (moon face, obesity, hirsutism, etc.) and possibly, when stopping treatment, to adrenal insufficiency (headaches, nausea, vertigo, etc.). Patients must be warned of accidental atomisation of the product in the eyes, which may cause irritation. The product should be used with caution and under the supervision of a physician in the case of patients suffering from prostatic hypertrophy and congenital porphyria. Caution is required in patients switching from treatment with systemic corticosteroids to a treatment with local corticosteroids, because of the possibility of adrenal insufficiency that can occur and allergies that can worsen (sometimes it may be necessary to apply a supplementary treatment in order to prevent some general symptoms caused by allergies). One should take into account a risk of infection with tuberculosis, with neurotropic viruses (herpes simplex, varicella-zoster, influenza) and opportunistic infections. In the case of bacterial, viral or mycotic infections of the upper respiratory tract, the mouth or eyes require specific treatment. After nasal administration of corticoids, systemic effects may occur, in particular when high doses are given for long periods of time. These effects are much less likely to occur than with oral corticosteroids and may vary between individual patients and between different corticosteroid preparations. Possible systemic effects could be Cushing's syndrome, Cushing-like features, adrenal gland suppression, growth retardation in children and adolescents, cataracts, glaucoma and less frequently, a series of psychological or behavioural effects, including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (especially in children). Growth retardation can be observed in children after nasal administration of the medicinal product. It is therefore advisable to regularly monitor the growth of children when they are treated nasally with corticoids for long periods of time. If growth has slowed down, the treatment should be adjusted and the administered dose of corticoids should be reduced to the lowest effective dose. In addition, advice of a specialist should be sought. Caution is required in patients with diabetes or osteoporosis. The use of vasoconstrictors requires caution in heart patients suffering from tachyarrhythmia, ischaemic heart disease, uncontrolled arterial hypertension or hyperthyroidism. Prolonged use of vasoconstrictors may give rise to iatrogenic rhinitis (hypertrophy of the nasal conchae, chronic nasal congestion, and atrophy of the mucosa). In the first place, it is recommended to rinse the nose with a saline solution; if the nasal congestion persists, the product can be used for up to 5 days.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (Pharmacovigilance): the prolonged use of corticosteroids in doses higher than those

recommended can give rise to systemic effects.

Immune system disorders: hypersensitivity reactions (rash, pruritus, urticaria). The signs of nose, throat and ear infections can be masked.

Endocrine disorders: hypercortisolism, growth retardation in children.

Mental disorders: hallucinations.

Nervous system disorders: headaches, fatigue (sedation, drowsiness), insomnia, agitation, vertigo, taste disorders.

Eye disorders: increase in intraocular pressure.

Heart disease: palpitations, tachycardia, rise in blood pressure, cardiac arrhythmia.

Respiratory system, chest and mediastinum disorders: burning sensation and dryness of the nasal mucous membrane, sneezing that may occur immediately after administration. Formation of scabs and irritation of the nose, ulceration and perforation of the nasal septum, nasal haemorrhage and irritation of the throat. After decreasing therapeutic effects, swelling of the nasal mucous membrane may occur.

GI disorders: nausea.

General disorders and administration site disorders: perspiration.

2.2 Indirect risks (incorrect use): by analogy with the other α-sympathicomimetics, the clinical picture of an intoxication with dexamethasone in combination with other active substances can cause confusion. Phases of stimulation and depression of the CNS and the cardiovascular system can alternate. In children an overdose can lead to epileptic seizures, coma, bradycardia, respiratory depression, a rise in blood pressure followed by a drop in blood pressure. The symptoms of CNS stimulation are anxiety, agitation, hallucinations and epileptic seizures. Symptoms of CNS depression are drop in body temperature, lethargy, sleepiness, coma. The following symptoms may also occur: sweating, anxiety, nausea, mydriasis, meiosis, swelling, fever, pallor, cyanosis of the lips, cardiovascular disorders (tachycardia, cardiac arrhythmia, bradycardia, cardiac arrest, hypertonia, blood pressure drop), respiratory disorders (respiratory insufficiency, respiratory arrest), psychological disorders.

Dexamethasone: chronic abuse can suppress the hypothalamo-pituitary-adrenal axis and thus give rise to signs of hypercorticism (moon face, obesity, etc.) and growth retardation in children.

In case of accidental overdose, the administration of activated carbon is one of the measures to be taken. In case of deliberate overdose, hospitalisation is required. The blood pressure and the body temperature should be monitored. Appropriate hypodermoclysis must be provided and, if necessary, mechanical ventilation.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	POM		0.25 mg/mL	3-5 times daily	3.37 mg (15 mL)
AT	Not authorised				
BE	POM	Short symptomatic treatment of inflammatory rhinitis (allergic rhinitis).	Combination product: tramazoline hydrochloride (0.12 mg) and		

		Adults and children 7 years and older	dexamethasone (0.02 mg)		
BiH	Not authorised				
CH	Not authorised				
CZ	Not authorised				
DE	Not authorised				
EE	Not authorised				
ES	Not authorised				
GE	Not subject to prescription				
HR	Not authorised				
IE	Not authorised				
IT	Not authorised				
LT	Not authorised				
MK	Not authorised				
PL	Not authorised				
PT	Not authorised				
RO	Not authorised				
RS	Not authorised				
SE	Not authorised				
SI	POM				

No more data available from other member states.

Melclass database[1]: Currently not available.

3.2 Social dimension of classification:

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

Proposed recommendation: **List I**

Criteria: not 1st line treatment of allergic rhinitis.

3.2.2 Paediatric use: not recommended in children under 7 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Federal Agency for Medicines and Health Products of Belgium (https://www.afmps.be/fr/items/banque_donnees)

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Tixocortol, Combinations

1.2 ATC code: R01AD57

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, medicines containing tixocortol in combination with other active substances are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Fluticasone, Combinations

1.2 ATC code: R01AD58

1.3 Therapeutic indications: relief of symptoms of moderate to severe seasonal and perennial allergic rhinitis if monotherapy with either intranasal antihistamine or glucocorticoid is not considered sufficient.

1.4 Posology and duration of treatment: adults and adolescents (12 years and older): one actuation in each nostril twice daily (morning and evening). The duration of treatment should correspond to the period of allergenic exposure.

Children below 12 years: this medicinal product is not recommended for use in children below 12 years of age as safety and efficacy has not been established in this age group.

1.5 Pharmaceutical forms: nasal spray suspension: 137 micrograms/50 micrograms per actuation, i.e. 137 micrograms azelastine hydrochloride (corresponding to 125 micrograms azelastine) and 50 micrograms fluticasone propionate.

1.6 Contraindications: hypersensitivity to the active substances or to any of the excipients.

1.7 Relevant warnings: during post-marketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression. Therefore, concomitant use of fluticasone and ritonavir should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side effects. Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Nasal sprays undergo extensive first-pass metabolism; therefore, the systemic exposure of intranasal fluticasone in patients with severe liver disease is likely to be increased. This may result in a higher frequency of systemic adverse events. Caution is advised when treating these patients. Treatment with higher than recommended doses of nasal corticosteroids may result in clinically significant adrenal suppression. If there is evidence for higher than recommended doses being used, then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery. In general the dose of intranasal fluticasone formulations should be reduced to the lowest dose at which effective control of the symptoms of rhinitis is maintained. Higher doses than the recommended one have not been tested for fluticasone. As with all intranasal corticosteroids, the total systemic burden of corticosteroids should be considered whenever other forms of corticosteroid treatment are prescribed concurrently. Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses. It is recommended that the growth of both children and adolescents receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid, if possible, to the lowest dose at which effective control of symptoms is maintained. Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as CSCR which have been reported after use of systemic and topical corticosteroids. Close monitoring is warranted in patients with a change in vision or with a history of increased ocular pressure, glaucoma and/or cataracts. In patients who have tuberculosis, any type of untreated infection, or have had a recent surgical operation or injury to the nose or mouth, the possible benefits of the treatment with the nasal spray should be weighed against possible risk. Infections of the nasal airways should be treated with antibacterial or antimycotic therapy, but do not constitute a specific contraindication to treatment with the nasal spray

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (Pharmacovigilance): commonly, dysgeusia, a substance-specific unpleasant taste, may be experienced after administration (often due to incorrect method of application, namely tilting the head too far backwards during administration).

An overview of adverse effects and their frequency is reported in the table below:

	Very common	Common	Uncommon	Rare	Very rare	Not known
Immune system disorders					Hypersensitivity including anaphylactic reactions, angioedema (oedema of the face or tongue and skin rash), bronchospasm	
Nervous system disorder		Headache, dysgeusia (unpleasant taste), unpleasant smell			Dizziness, somnolence (drowsiness, sleepiness)	
Eye disorders*					Glaucoma, increased intraocular pressure, cataract	Blurred vision
Respiratory, thoracic and mediastinal disorders	Epistaxis		Nasal discomfort (including nasal irritation, stinging, itching), sneezing, nasal dryness, cough, dry throat, throat irritation		Nasal septal perforation, mucosal erosion	Nasal ulcers
GI disorders				Dry mouth	Nausea	
Skin and subcutaneous tissue disorders					Rash, pruritus, urticaria	
General disorders and administration site conditions					Fatigue (weariness, exhaustion), weakness	

2.2 Indirect risks (incorrect use): with the nasal route of administration overdose reactions are not anticipated. There are no data from patients available on the effects of acute or chronic overdosage with intranasal fluticasone. Intranasal administration of 2 milligrams fluticasone (10 times the recommended daily dose) twice daily for 7 days to healthy human volunteers had no effect on HPA-axis function. Administration of doses higher than those recommended over a long period of time may lead to temporary suppression of adrenal function. In these patients, treatment should be continued at a dose sufficient to control symptoms; the adrenal function will recover in a few days and can be verified by measuring plasma cortisol. In the event of overdose after incidental oral uptake, disturbances of the CNS (including drowsiness, confusion, coma, tachycardia and hypotension) caused by azelastine hydrochloride are to be expected based on the results of animal experiments. Treatment of these disorders must be symptomatic. Depending on the amount swallowed, gastric lavage is recommended. There is no known antidote.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	POM		50 mcg/dose	twice daily	6000 mcg/120 doses (23 g bottle)
AT	List I	Allergic rhinitis	125 mcg into each nostril	250 mcg into each nostril	N.A.
BE	Not authorised				
BiH	POM	Relief of symptoms of moderate to severe seasonal and perennial allergic rhinitis	50 mcg/dose fluticasone + 137 mcg/dose azelastine hydrochloride		
CH	List II				
DE	POM				
ES	POM				
GE	Not subject to prescription				
HR	List II	Relief of symptoms of moderate to severe seasonal and perennial allergic rhinitis if monotherapy with either intranasal antihistamine or glucocorticoid is not considered sufficient (in adults and adolescents above 12 years).	137 mcg + 50 mcg per actuation	2 x 1 actuation into each nostril	
IE	List II				
IT	List II				
LT	POM				
MK	Not authorised				
PL	POM				
PT	POM				
RO	List I	Relief of seasonal and perennial allergic symptoms moderate to severe if monotherapy with intranasal antihistamines or glucocorticoids is not considered sufficient.	137 mcg + 50 mcg/dose	250 mcg + 50 mcg	120 doses
RS	POM				
UK	POM				

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

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

Proposed recommendation: **List I**

Criteria: not 1st line treatment (to be used when monotherapy with either intranasal antihistamine or glucocorticoid is not considered sufficient).

3.2.2 Paediatric use: this combination product is not recommended for use in children below 12 years of age.

3.2.3 Social dimension: -

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

4. REFERENCES/COMMENTS

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

Irish Health Products Regulatory Authority (https://www.hpra.ie/homepage/medicines)

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1.Active ingredient: Hydrocortisone, Combinations

1.2 ATC code: R01AD60

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing hydrocortisone in combination with other active substances are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Calcium Hexamine Thiocyanate

1.2 ATC code: R01AX01

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Retinol

1.2 ATC code: R01AX02

1.3 Therapeutic indications: local symptomatic relief of nasal mucosal irritation in dry nasal colds with or without crust formation in the nostrils, in adults and children over 6 years of age.

1.4 Posology and duration of treatment: adults and children over 6 years: a small amount should be applied 2 or 3 times a day in the affected area.

1.5 Pharmaceutical forms: 12,500 IU/g nasal ointment.

1.6 Contraindications: hypersensitivity to retinol or to any of the excipients.

1.7 Relevant warnings: retinol should not be administered to children under 6 years of age. If the symptoms do not improve after 10 days of treatment, the diagnosis should be reconsidered.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): none described under the authorised conditions of use.

2.2 Indirect risks (incorrect use): none stated.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not authorised				
BE	Not authorised				
BiH	Not authorised				
CH	Not subject to prescription				
CZ	Not authorised				
DE	Not subject to prescription				
ES	Not subject to prescription				
GE	Not authorised				
HR	Not authorised				
HU	Not authorised				
IE	Not authorised				
IT	Not authorised				
LT	Not authorised				
MK	Not authorised				
NL	Not authorised				
PL	Not authorised				
PT	Not authorised				
RO	Not authorised				
RS	Not authorised				
SE	Not authorised				
SI	Not authorised				

No more data available from other member states.

Melclass database[1]: -

3.2 Social dimension of classification:

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

Proposed recommendation: **Not subject to prescription** (nasal use).

Criteria: well-known pharmacological profile.

3.2.2 Paediatric use: children above 6 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: SmPC from Spanish Agency for Medicines and Health Products (https://cima.aemps.es/cima/dochtml/ft/28811/FT_28811.html)

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Ipratropium Bromide

1.2 ATC code: R01AX03

1.3 Therapeutic indications: indicated for the symptomatic relief of rhinorrhoea in allergic and non-allergic rhinitis.

1.4 Posology and duration of treatment: adults: 2 sprays (2 x 21 micrograms = 42 micrograms) in each nostril administered 2-3 times a day.

Children: the use of this product has not been evaluated in children; therefore, it is not recommended for use in patients below the age of 12 years.

1.5 Pharmaceutical forms: nasal spray solution, 21 micrograms per metered dose.

1.6 Contraindications: contraindicated in patients known to be hypersensitive to atropine or its derivatives or to any other component of the product. Non-prescription product is contraindicated in under 6 years in Belgium.

1.7 Relevant warnings: immediate hypersensitivity reactions following the use of this product have been demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, oropharyngeal oedema and anaphylaxis. Caution is advocated in the use of anticholinergic agents in patients predisposed to narrow-angle glaucoma, or with pre-existing urinary outflow tract obstruction (e.g. prostatic hyperplasia or bladder-outflow obstruction). As patients with cystic fibrosis may be prone to GI motility disturbances, this product, as with other anticholinergics, should be used with caution in these patients. There have been isolated reports of ocular complications (i.e. mydriasis, increased intraocular pressure, angle-closure glaucoma, eye pain) when aerosolised ipratropium bromide, either alone or in combination with an adrenergic beta2- agonist, has come into contact with the eyes. Thus patients must be instructed in the correct administration of this product. Eye pain or discomfort, blurred vision, visual halos or coloured images in association with red eyes from conjunctival congestion and corneal oedema may be signs of acute narrow-angle glaucoma. Should any combination of these symptoms develop, treatment with miotic drops should be initiated and specialist advice sought immediately.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): the most frequent side effects reported in clinical trials were epistaxis, nasal dryness, headache, nasal discomfort and throat irritation.

Immune system disorders, nervous system disorders and eye disorders: common: headache; uncommon: hypersensitivity, anaphylactic reactions, dizziness, blurred vision, mydriasis, intraocular pressure increased, glaucoma, eye pain, halo vision, conjunctival hyperaemia, corneal oedema, accommodation disorder.

Cardiac disorders: uncommon: supraventricular tachycardia, atrial fibrillation, heart rate increased; rare: palpitations.

Respiratory, thoracic and mediastinal disorders: common: epistaxis, nasal dryness, throat irritation, nasal discomfort; uncommon: dry throat, bronchospasm, laryngospasm, pharyngeal oedema.

GI disorders: uncommon: dry mouth, nausea, GI motility disorder, stomatitis, oedema mouth.

Skin and subcutaneous tissue disorders: uncommon: rash, angioedema, urinary retention; rare: urticaria, pruritus.

Notes: 1) Ocular complications have been reported when aerolised ipratropium bromide, either alone or in combination with an adrenergic beta2-agonist, has come into contact with the eyes. 2) The risk

of urinary retention may be increased in patients with pre-existing urinary outflow tract obstruction.

2.2 Indirect risks (incorrect use): no symptoms specific to overdosage have been encountered. In view of the wide therapeutic window and topical administration of this product, no serious anticholinergic symptoms are to be expected. As with other anticholinergics, dry mouth, visual accommodation disorder and tachycardia would be the expected symptoms and signs of overdose.

2.3 Recent cases at European level: none

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not authorised				
BE	Not subject to prescription	Symptomatic treatment of rhinorrhoea in allergic and non-allergic rhinitis. Adults and children 6 years and older.	0.3 mg/mL		
BiH	Not authorised				
CH	List II				
CZ	Not authorised				
DE	Not authorised				
ES	POM				
GE	Not authorised				
HR	Not authorised				
HU	Not authorised				
IE	List II				
IT	List II				
LT	Not authorised				
MK	Not authorised				
NL	Not authorised				
PL	Not authorised				
PT	Not authorised				
RO	Not authorised				
RS	Not authorised				
SE	POM + Exemption		Ex.: 21 mcg/dose		Ex.: 15 mL (180 doses)
SI	POM				

No more data available from other member states.

Melclass database[1]: List II

3.2 Social dimension of classification:

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

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

Proposed recommendation: **List II**

Criteria: medicinal product which requires long-term use.

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: SmPC HPRA:
https://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA0007-027-002_04082017140054.pdf

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Ritiometan

1.2 ATC code: R01AX05

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, no medicines containing this active substance are authorised in member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Mupirocin

1.2 ATC code: R01AX06

1.3 Therapeutic indications: indicated for the treatment of nasal carriage of staphylococci, including methicillin-resistant *Staphylococcus aureus* (MRSA). Consideration should be given to official guidance on the appropriate use of antibacterial agents.

1.4 Posology and duration of treatment: nasal ointment should be applied to the anterior nares two to three times a day, as follows: a small amount of the ointment about the size of a match head is placed on the little finger and applied to the inside of each nostril. The nostrils are closed by pressing the sides of the nose together; this will spread the ointment throughout the nares. A cotton bud may be used instead of the little finger for the application in particular to infants or patients who are very ill. Nasal carriage should normally clear within 5-7 days of commencing treatment.

1.5 Pharmaceutical forms: nasal ointment 2% w/w

1.6 Contraindications: hypersensitivity to the active substance or to any of the excipients.

1.7 Relevant warnings: in the rare event of a possible sensitisation reaction or severe local irritation occurring with the use of the product, treatment should be discontinued, the product should be wiped off and appropriate alternative therapy for the infection instituted. As with other antibacterial products, prolonged use may result in overgrowth of non-susceptible organisms. Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. Although this is less likely to occur with topically applied mupirocin, if prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further. This mupirocin formulation is not suitable for ophthalmic use. Contact with the eyes should be avoided. If contaminated, the eyes should be thoroughly irrigated with water until the ointment residues have been removed.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): uncommon adverse reactions were determined from pooled safety data from a clinical trial population of 422 treated patients encompassing 12 clinical studies. Very rare adverse reactions were primarily determined from post-marketing experience data and therefore refer to reporting rate rather than true frequency.

Immune system disorders: very rare: cutaneous hypersensitivity reactions; systemic allergic reactions including anaphylaxis, generalised rash, urticaria and angioedema.

Respiratory, thoracic and mediastinal disorders: uncommon: nasal mucosa reactions.

2.2 Indirect risks (incorrect use): symptoms: there is currently limited experience with overdosage of mupirocin. Management: there is no specific treatment for an overdose of mupirocin. In the event of overdose, the patient should be treated supportively with appropriate monitoring as necessary. Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

2.3 Recent cases at European level: none

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not authorised				
BE	Not authorised				
BiH	Not authorised				
CH	List I				
CZ	POM				
DE	POM				
ES	Not authorised				
GE	Not authorised				
HR	Not authorised				
HU	POM				
IE	List I				
IT	List II				
LT	Not authorised				
LV	Not authorised				
MK	POM				
NL	POM				
PL	POM	Nasal ointment 20 mg/g			
PT	Not authorised				
RO	Not authorised				
RS	Not authorised				
SE	Not authorised				
SI	POM				

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

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

Proposed recommendation: **List I**

Criteria: antibacterial agent which requires short-term treatment and medical supervision.

3.2.2 Paediatric use: the safety and efficacy of mupirocin in children under one year of age has not been established.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: SmPC HPRA:
https://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1077-094-002_24012017151116.pdf

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Hexamidine

1.2 ATC code: R01AX07

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are only authorised in Switzerland (legal status: not subject to prescription)).

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Framycetin

1.2 ATC code: R01AX08

1.3 Therapeutic indications: adjunctive treatment of infections of the nasal mucosa, nasopharyngeal mucosa and paranasal sinuses. Prophylaxis treatment in rhinological surgery. The treatment should be of short duration (no more than 10 days).

1.4 Posology and duration of treatment: adults: 3 to 5 drops in each nostril, 3 to 4 times a day. Children: 1 to 2 drops in each nostril, 3 to 4 times a day. Babies up to 2 years: 1 drop in each nostril, 3 to 4 times a day.

1.5 Pharmaceutical forms: 7800 IU/mL nasal spray and nasal drops.

1.6 Contraindications: hypersensitivity to the active substance or to any of the excipients; allergy to antibiotics of the aminoglycoside group (framycetin)

1.7 Relevant warnings: caution is recommended in the elderly and in people with kidney failure or prior hearing impairment. The treatment should not last more than 10 days.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): the nasal route administration of framycetin may induce an allergy to antibiotics of the aminoglycoside group. Although nasally administered doses are extremely low, the following adverse reactions associated with the use of higher doses of the aminoglycosides have been observed:

Ototoxicity: vestibular and auditory damage has been described in the literature following the administration of aminoglycosides; elderly patients are more sensitive to these effects as well as those with pre-existing hearing impairment.

Nephrotoxicity: cases of nephrotoxicity with aminoglycosides have been reported. An increase in uraemia has been observed, which usually returns to normal soon or immediately after stopping treatment. Cases of renal impairment after administration of aminoglycosides were in most of the cases reported in connection with excessively high dosage or prolonged treatment, in patients with history of renal impairment, patients suffering from hemodynamic disorders or patients using medicinal products known to be potentially nephrotoxic. Nephrotoxicity may be potentiated by certain drugs. The potential nephrotoxicity of cephalosporins and in particular cefaloridine may be increased in the presence of aminoglycosides. If this combination is initiated, the monitoring of renal function is recommended. Elderly people are also more likely to suffer kidney damage.

Neuromuscular blockade and respiratory paralysis have been reported with the administration of this medication to patients who have received curare-type substances during anaesthesia with a muscle relaxant effect.

Effects on the central nervous system and peripheral neuritis have also been observed.

2.2 Indirect risks (incorrect use): no risks of overdosage expected as nasal and GI resorption of framycetin is extremely low.

2.3 Recent cases at European level: none stated

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	POM		8000 IU/mL	4-6 times daily	120000 IU (15mL)
AT	Not authorised				
BE	Not subject to prescription	Adjuvants for infections of nasal mucosa, rhino pharynx and sinus with permeable ostium	7800 IU		
BiH	Not authorised				
CH	Not authorised				
CZ	Not authorised				
DE	Not authorised				
ES	Not authorised				
GE	Not subject to prescription				
HR	Not authorised				
HU	Not authorised				
IE	Not authorised				
IT	Not authorised				
LT	Not authorised				
MK	Not authorised				
NL	Not authorised				
PL	Not authorised				
PT	Not authorised				
RO	Not authorised				
RS	Not authorised				
SE	Not authorised				
SI	Not authorised				

No more data available from other member states.

Melclass database[1]: -

3.2 Social dimension of classification:

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

Proposed recommendation: **List I**

Criteria: short-term treatment; medical supervision required.

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Federal Agency for Medicines and Health Products of Belgium (https://www.afmps.be/fr/items/banque_donnees)

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Hyaluronic Acid

1.2 ATC code: R01AX09

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, medicines containing this active substance are only authorised in Switzerland (legal status: not subject to prescription)).

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Various

1.2 ATC code: R01AX10

1.3 Therapeutic indications: facilitate nasal breathing with obstructed nose (AT). Symptomatic treatment of flu and cold conditions, nasal congestion and rhinorrhoea (PT).

1.4 Posology and duration of treatment: no longer than 7 days.

1.5 Pharmaceutical forms: various pharmaceutical forms depending on the combination products that are authorised in the member states.

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not subject to prescription				
AT	Not subject to prescription	Indicated to facilitate nasal breathing with obstructed nose.			
BE	Not authorised				
BiH	Not authorised				
CH	Not subject to prescription				
CZ	Not subject to prescription				
DE	Not authorised				
ES	Not subject to prescription				
GE	Not subject to prescription				
HR	Not authorised				
HU	Not subject to prescription				
IE	Not authorised				
IT	List II + Exemption	List II: combination product: meomycin, eucalyptol, pine essence, camphor, menthol, chlorobutanol) Ex.: combination product containing colloidal silver			
LT	Not authorised				

LV	Not subject to prescription				
MK	Not authorised				
NL	Not authorised				
PL	Not authorised				
PT	Not subject to prescription	Symptomatic treatment of flu and cold conditions, nasal congestion and rhinorrhoea	0.25 mg/mL + 2.5 mg/mL (Dimetindene + Phenylephrine)		
RO	Not subject to prescription				
RS	Not authorised				
SE	Not authorised				
SI	Not subject to prescription				

No more data available from other member states.

Melclass database[1]: -

3.2 Social dimension of classification:

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

Proposed recommendation: **Not to classify**

Criteria: the WHO ATC code database states: **"**ATC level R01AX10 is an old level where rather obsolete nasal preparations and sodium chloride nasal products are classified. The level R01AX30 is for nasal combination products which cannot be classified in the preceding groups." In conclusion, no classification is recommended as this ATC code is now obsolete. Countries with products with this ATC code may wish to consider migrating such products to ATC code R01AX30.

3.2.2 Paediatric use: N.A.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: WHO ATC codes R01AX10 and R01AX30:
https://www.whocc.no/atc_ddd_index/?code=R01AX30&showdescription=yes

Databases of national competent authorities.

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Combinations

1.2 ATC code: R01AX30

1.3 Therapeutic indications: AT: adjuvant treatment of rhinitis as of 6 years; permanent treatment of ozaena, pharyngitis sicca, pharyngitis sicca chronica; treatment of wounds after nasal surgery.

BE: symptomatic treatment of nasal congestion in allergic rhinitis, vasomotor rhinitis, sinusitis, pre- and post-operative treatment in case of nasal surgery.

IE: in the relief of symptoms of nasal congestion associated with allergic and infectious upper respiratory tract disorders.

1.4 Posology and duration of treatment: adults and children over 6 years: medicinal products belonging to this ATC code are used by inserting the inhaler into each nostril, holding the other nostril closed and inhaling deeply. They can be used as frequently as needed. They are not recommended in children under 6 years of age.

1.5 Pharmaceutical forms: nasal sticks and nasal drops.

1.6 Contraindications: patients hypersensitive to any of the ingredients.

1.7 Relevant warnings: if there is no improvement or aggravation of the disorder a physician should be consulted.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): in general no serious or severe side effects are expected with this product. Very rarely cases of nasal discomfort have been reported.

2.2 Indirect risks (incorrect use): no clinically significant cases of overdose have been reported.

2.3 Recent cases at European level: none

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not subject to prescription	Adjuvant treatment of rhinitis as of 6 years; permanent treatment of ozaena, pharyngitis sicca, pharyngitis chronica sicca; treatment of wounds after nasal surgery	2 drops into each nostril	6 drops into each nostril	N.A.
BE	Not subject to prescription	Symptomatic treatment of nasal congestion in allergic rhinitis, vasomotor rhinitis, sinusitis, pre- and post-operative in case of nasal surgery	0.25 mg dimetindene maleate 2.5 mg phenylephrine/mL		
BiH	Not authorised				
CH	Not authorised				
DE	Not authorised				
GE	Not subject to prescription				

IE	Not subject to prescription (general sale)	In the relief of symptoms of nasal congestion such as are associated with allergic and infectious upper respiratory tract (menthol, camphor, Siberian Pine needle oil). If there is no improvement or aggravation of the disorder consult the doctor. Adults and children over 6 years.			Inhaler nasal stick - menthol 125 mg + camphor 50 mg + Siberian pine needle oil 10 mg
IT	Not subject to prescription				
LT	POM				
MK	Not authorised				
PL	Not authorised				
PT	Not authorised				
RO	Not authorised				
RS	Not authorised				

No more data available from other member states.

Melclass database[1]: -

3.2 Social dimension of classification:

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

Proposed recommendation: **Not to classify**

Criteria: it is unclear which nasal combination products are classified under this ATC code.

3.2.2 Paediatric use: N.A.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: databases of national competent authorities.

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Phenylpropanolamine

1.2 ATC code: R01BA01

1.3 Therapeutic indications: allergic and vasomotor rhinitis with mucosal swelling when local treatment does not have adequate effect.

1.4 Posology and duration of treatment: oral, short term treatment.

1.5 Pharmaceutical forms: 25 mg prolonged-release tablets, 50 mg prolonged-release tablets.

1.6 Contraindications: hypertonia, cardiovascular disease, bronchial asthma, chronic obstructive lung disease, pneumonia, respiratory insufficiency, respiratory depression, severe liver and renal impairment, phaeochromocytoma, prostate adenoma, glaucoma, hyperthyreosis, diabetes mellitus, treatment with MAOIs, pregnancy and lactation.

1.7 Relevant warnings: anomalous heart frequency, Gilbert syndrome, renal damage, liver disorder due to toxic hepatitis.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): adverse reactions occur in 5-20% of treated patients.

Mental disorders: common: nervousness; rare: nightmares, aggression, confusion, hallucinations.

Central and peripheral nervous system: common: sleeping difficulties.

Respiratory, chest and the mediastinum: common: dry sensation in the nose.

GIdisorders: common: mouth dryness.

Kidneys and urinary tract: common: micturition difficulties, urinary retention.

Skin and subcutaneous tissue: uncommon: hypersensitivity reactions (urticaria, exanthema, itching).

Vascular: rare: transient blood pressure rise; very rare: intracranial bleeding.

2.2 Indirect risks (incorrect use): increase of intraocular pressure, nausea, GI discomfort, diarrhoea, vomiting, loss of appetite, nervousness, tremor, restlessness, agitation, anxiety, dizziness, hallucinations, slight tiredness or insomnia, headache, dizziness, in abuse development of dependence, urinating disorders, increase in liver transaminases, palpitations, tachycardia, blood pressure increase or decrease, cardiovascular disorders, stroke, skin reactions Quincke's oedema, drop in blood pressure to shock (first signs may be: sweating, nausea, dizziness, vomiting), thrombocytopenia, agranulocytosis, haemolytic anaemia, neutropenia, leukopenia, pancytopenia.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				

AT	Not authorised				
BE	Not authorised				
BiH	Not authorised				
CH	Not authorised				
CZ	Not authorised				
DE	Not authorised				
EE	Not authorised				
ES	Not authorised				
FI	POM	Indication: vasomotor rhinitis. Mild to moderate sensory stress and urinary incontinence in postmenopausal women with severe stress incontinence. Over 12 years and adults: 1 tablet in the morning and evening. The prolonged-release tablet should not be halved or chewed, but should be swallowed whole.	50 mg	50 mg	
FR	Not authorised				
GE	Not authorised				
HR	Not authorised				
HU	Not authorised				
Iceland (IS)	POM	Allergic rhinitis. Vasomotor motor rhinitis, when patients are particularly disturbed by nasal congestion.			
IE	Not authorised				
IT	Not authorised				
LT	Not authorised				
LV	Not authorised				
MK	Not authorised				
NL	Not authorised				
NO	POM	Allergic and vasomotor rhinitis with mucosal swelling when local treatment does not have adequate effect.	50 mg	100 mg	
PL	Not authorised				
PT	Not authorised				
RO	Not authorised				
RS	Not authorised				
SE	POM	Allergic mucosal swelling of the nose. Vasomotor rhinitis when the patient mainly has problems with nasal congestion.	50 mg	100 mg	
SI	Not authorised				
UK	Not authorised				

No more data available from other member states.

Melclass database[1]: List I

3.2 Social dimension of classification:

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

Proposed recommendation: **List I**

Criteria: short-term treatment; not 1st line treatment.

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

3.2.2 Paediatric use: children under 12 years of age: MS 25 mg, MDD 50 mg. Not for children under 5 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference - 37th Edition

Swedish Medical Products Agency - https://bit.ly/3a6C8Ur

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Pseudoephedrine

1.2 ATC code: R01BA02

1.3 Therapeutic indications: indicated for the relief of nasal, sinus and upper respiratory congestion.

1.4 Posology and duration of treatment: oral, short-term treatment.

1.5 Pharmaceutical forms: tablets for oral use.

1.6 Contraindications: patients with cardiovascular disease including ischaemic heart disease, occlusive vascular disease and hypertension. Children under 12 years of age. Patients with severe renal impairment, phaeochromocytoma, diabetes, hyperthyroidism, closed-angle glaucoma.

1.7 Relevant warnings: caution should be used when prescribing pseudoephedrine for patients with prostatic enlargement or bladder dysfunction. Also use with caution in patients with severe hepatic impairment or with mild to moderate renal impairment. If any of the following occur, the use should be stopped: hallucinations, restlessness, sleep disturbances. Patients with rare hereditary problems of galactose intolerance, the LAPP lactase deficiency or glucose-galactose malabsorption should not take pseudoephedrine.

Severe skin reactions: severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) may occur with pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localised on the skin folds, trunk and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema or many small pustules are observed, administration of pseudoephedrine should be discontinued and appropriate measures taken if needed.

Ischaemic colitis: some cases of ischaemic colitis have been reported with pseudoephedrine. Pseudoephedrine should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): adverse effects may include dry mouth, anxiety, restlessness, tremor, insomnia, tachycardia, cardiac arrhythmias, palpitations, hypertension, nausea, vomiting, headache and occasionally urinary retention in males and skin rashes. Hallucinations have been reported rarely, particularly in children. Skin and subcutaneous tissue disorders: frequency unknown: severe skin reactions, including acute generalised AGEP.

2.2 Indirect risks (incorrect use): caution should be exercised with patients receiving other sympathomimetic agents (e.g. avoid use with apraclonidine), appetite suppressants or other amphetamine-like psychostimulants, as there is a risk of hypertension. Pseudoephedrine may antagonise the effects of antihypertensive agents, such as adrenergic neurone blockers, and severe hypertension may occur in patients receiving beta-blockers. Hypertensive crisis may occur if pseudoephedrine is co-administered with MAOIs. Concomitant use of pseudoephedrine should be avoided with MAOIs including rasagiline and selegiline, or reversible inhibitors of monoamine oxidase A (RIMAs) such as moclobemide. There may be increased risk of arrhythmias if pseudoephedrine is given to patients receiving cardiac glycosides, quinidine, volatile anaesthetics such as cyclopropane, or halothane, or anticholinergic drugs such as tricyclic antidepressants. Pseudoephedrine also increases the risk of ergotism if used with ergot alkaloids, ergotamine and methysergide. The effects of pseudoephedrine may be antagonised by antipsychotics and its absorption rate may be reduced by kaolin. The effects of pseudoephedrine may be increased by doxapram and oxytocin (as there is a risk of hypertension) and its absorption may be increased by aluminium hydroxide. The antibacterial agent furazolidone is known to cause progressive inhibition of monoamine oxidase (a metabolite of furazolidone is a MAOI). Although there have been no reports of hypertensive crisis, it may not be administered concurrently with pseudoephedrine.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	Not subject to prescription				
BE	POM + Exemption	Ex.: oral use	Ex.: 60 mg		
BG	Not authorised				
BiH	Not authorised				
CH	List II				
CZ	Not authorised				
DE	POM + Exemption	Ex.: oral use	Ex.: 60 mg		
EE	Not subject to prescription				
ES	Not subject to prescription				
FI	Not authorised				
FR	Not authorised				
GE	Not authorised				
HR	Not authorised				
HU	Not authorised				
IE	Not subject to prescription				
IT	Not authorised				
LT	Not authorised				
LV	Not authorised				
MK	Not authorised				
NL	Not authorised				
PL	Not subject to prescription				
PT	Not authorised				
RO	Not subject to prescription				
RS	Not authorised				
SE	Not authorised				
SI	Not authorised				
UK	POM + Exemption	Ex.: oral use	Ex.: 60 mg	Ex.: 240 mg	Ex.: 720 mg

No more data available from other member states.

Melclass database[1]: List II + Exemption (exemptions: oral use; MS: 60 mg).

3.2 Social dimension of classification:

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

Proposed recommendation: **List II + Exemption**

Exemptions: oral use; MS: 60 mg; MDD: 240 mg; MQP: 720 mg; short-term use (max 3 days).

Criteria: under the exemptions stated, the use of the product is considered to be safe; known use; self-

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

assessment possible; medical advice to be sought after 3 days of use if symptoms do not improve or worsen.

3.2.2 Paediatric use: prescription-only for children under 12 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference - 37th Edition; databases of national competent authorities.

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Phenylephrine

1.2 ATC code: R01BA03

1.3 Therapeutic indications: -

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing this active substance are authorised in member states, except for Poland where medications containing phenylephrine are classified as Not subject to prescription).

3.2 Social dimension of classification:

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

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

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Phenylpropanolamine, Combinations

1.2 ATC code: R01BA51

1.3 Therapeutic indications: common cold with cough, rhinitis, headache, musculoskeletal pain, moderate fever, nasal and pharyngeal mucosa swelling.

1.4 Posology and duration of treatment: -

1.5 Pharmaceutical forms: -

1.6 Contraindications: -

1.7 Relevant warnings: -

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): -

2.2 Indirect risks (incorrect use): -

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications (ATC codes) and supply conditions: no data (based on the available data, no medicines containing phenylpropanolamine in combination with other active substances are authorised in member states, except for Germany where medications containing phenylephrine are classified as Not subject to prescription).

3.2 Social dimension of classification:

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

Proposed recommendation: based on the available data, medicines containing phenylpropanolamine in combination with other active substances are not authorised in at least three member states: **Not to classify**

3.2.2 Paediatric use: -

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: -

4.2 Comments: -

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Pseudoephedrine, Combinations

1.2 ATC code: R01BA52

1.3 Therapeutic indications: relief of symptoms of cold and flu with associated congestion, including aches and pains, headache, fever, sore throat, blocked nose and sinuses.

1.4 Posology and duration of treatment: oral, short-term treatment. The patient should consult a doctor if symptoms persist or worsen, or if treatment is required for more than 10 days.

1.5 Pharmaceutical forms: tablets containing 30 mg pseudoephedrine; MS: 30-60 mg, MDD: 180 mg; not for children under 12. Various combination products with a valid marketing authorisation in member states: pseudoephedrine and desloratadine; pseudoephedrine and loratadine; pseudoephedrine and cetirizine; pseudoephedrine and ibuprofen; pseudoephedrine and triprolidine; pseudoephedrine, triprolidine and paracetamol; pseudoephedrine and chlorpheniramine; pseudoephedrine, triprolidine and dextromethorphan; pseudoephedrine and acetylsalicylic acid.

1.6 Contraindications: patients with cardiovascular disease including ischaemic heart disease, occlusive vascular disease and hypertension. Children under 12 years of age. Patients with severe renal impairment, phaeochromocytoma, diabetes, hyperthyroidism, closed-angle glaucoma.

1.7 Relevant warnings: see pseudoephedrine (ATC code: R01BA02).

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): associated with pseudoephedrine:

Cardiovascular disorders: tachycardia, palpitations, other cardiac dysrhythmias.

GI disorders: nausea and/or vomiting, dry mouth.

General disorders and administration site conditions: irritability, thirst, tolerance with dependence has been reported with prolonged administration of pseudoephedrine-containing preparations.

Immune system disorders: hypersensitivity reactions, including cross-sensitivity that may occur with other sympathomimetics.

Musculoskeletal and connective tissue disorders: muscular weakness. Nervous system disorders: headache, giddiness, tremor, anxiety, restlessness, excitability, insomnia, hallucinations (particularly in children) and paranoid delusions.

Psychiatric disorders: sleep disturbance.

Renal and urinary disorders: difficulty in micturition including urinary retention.

Skin and subcutaneous tissue disorders: skin reactions including rash, sweating. Frequency unknown - severe skin reactions, including AGEP.

Vascular disorders: hypertension.

Other side effects can be experienced depending on the active substances included in the combination product.

2.2 Indirect risks (incorrect use): see pseudoephedrine (ATC code: R01BA02).

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

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

Country	Classification	Additional information			
		Routes of administration/ Indications	MS	MDD	MQP
AM	Not authorised				
AT	List II + Exemption	Not for children under 16	Ex.: 60 mg	Ex.: 240 mg	
BE	POM + Exemption	Ex.: Oral use		Ex.: 240 mg	
BG	Not subject to prescription				
BiH	Not subject to prescription				
CH	Not authorised				
CZ	POM				
EE	POM				
ES	Divergent classification status				
FI	Not authorised				
FR	Not subject to prescription				
GE	POM				
HR	List I + Exemption	List I: combination with desloratadine. Other combinations are non-prescription.			
HU	POM + Exemption	POM: combination with cetirizine Non-prescription: combination with ibuprofen			
IE	Not subject to prescription				
IT	List II + Exemption	Ex.: pseudoephedrine (MS 60 mg) + triprolidine (MS 2.5 mg); pseudoephedrine (MS 60 mg) + triprolidine (MS 2.5 mg) + paracetamol (MS 300 mg); pseudoephedrine (MS 30 mg) + ibuprofen (MS 200 mg); pseudoephedrine (MS 120 mg) + cetirizine (MS 5 mg)			
LT	POM + Exemption	Ex.: pseudoephedrine (MS: 60 mg) and triprolidine (MS: 2.5 mg)			
LV	POM + Exemption	Ex.: pseudoephedrine (MS: 60 mg) and triprolidine (MS: 2.5 mg); pseudoephedrine (MS: 30 mg) and chlorpheniramine (MS: 2 mg).			
MK	Not subject to prescription				
NL	POM				
PL	POM + Exemption	Ex.: 30 mg pseudoephedrine + 1.25 mg triprolidine + 10 mg dextromethorphan/5 mL; MS 30 mg pseudoephedrine + 200 mg of ibuprofen; 120 mg pseudoephedrine + 5 mg of cetirizine.			
PT	POM + Exemption	Ex.: loratadine (MS: 5 mg) + pseudoephedrine (MS: 120 mg); Pseudoephedrine (MS: 60			

		mg) + triprolidine (MS: 2.5 mg).			
RO	Not subject to prescription				
RS	POM + Exemption	Ex.: pseudoephedrine (MS: 60 mg) in combination with ibuprofen (MS: 400 mg); pseudoephedrine (MS: 60 mg) in combination with triprolidine (MS: 2.5 mg); pseudoephedrine (MS: 30 mg) in combination with acetylsalicylic acid (MS: 500 mg).			
SE	POM				
SI	Not subject to prescription				
UK	POM + Exemption	Ex.: Oral use	Ex.: 60 mg	Ex.: 180 mg	

No more data available from other member states.

Melclass database[1]: Currently not available.

3.2 Social dimension of classification:

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

Proposed recommendation: **List II + Exemption**

Exemptions: oral use; MS: 60 mg of pseudoephedrine; MDD: 240 mg of pseudoephedrine; MQP: 720 mg of pseudoephedrine; short-term use.

Criteria: under the exemptions stated, the use of the product is considered to be safe; known use; self-assessment possible; medical advice to be sought after 3 days of use if symptoms do not improve or worsen.

3.2.2 Paediatric use: prescription-only for children under 12 years of age.

3.2.3 Social dimension: -

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference - 37th Edition; databases of national competent authorities.

4.2 Comments: -

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

1. THERAPEUTIC PROFILE

1.1 Active ingredient: Phenylephrine, Combinations

1.2 ATC code: R01BA53

1.3 Therapeutic indications: short-term symptomatic treatment of colds and influenza (aches and/or fever) when associated with nasal congestion.

1.4 Posology and duration of treatment: oral, short-term treatment.

Adults: 1 sachet dissolved by stirring in hot water. The dose may be repeated in 4-6 hours. No more than 4 doses should be taken in 24 hours.

Paediatric population: children under 16 years of age: not recommended for use in children below the age of 16 years without medical advice.

Children over 16 years of age: 1 sachet dissolved by stirring in hot water. The dose may be repeated in 4-6 hours. No more than 4 doses should be taken in 24 hours.

1.5 Pharmaceutical forms: powder for oral solution, MS: 10 mg of phenylephrine.

1.6 Contraindications: severe coronary heart disease, hypertension, glaucoma, hyperthyroidism, use in patients taking tricyclic antidepressants, use in patients who are currently taking or have taken MAOIs within the last 2 weeks, severe impairment of liver function, acute hepatitis, alcohol abuse.

1.7 Relevant warnings: use with caution in patients with Raynaud's phenomenon, diabetes, moderate and severe renal insufficiency, liver function disorders (mild to moderate hepatocellular insufficiency (including Gilbert's syndrome), concomitant treatment with medicinal products affecting hepatic functions), haemolytic anaemia, dehydration, chronic malnutrition, glutathione depletion due to metabolic deficiencies, prostatic hypertrophy, phaeochromocytoma.

2. LIST DIRECT/INDIRECT RISKS (SAFETY PROFILE)

2.1 Direct risks (pharmacovigilance): exceptionally drowsiness. Rarely, blood dyscrasias, increased sensitivity of the skin to the sun, increased sweating and loss of appetite may occur. Also with a rare incidence, a paradoxical reaction (nightmares, excitement, nervousness, etc.) may occur, more likely in children and in elderly patients; these patients are also more likely to experience confusion, difficulty or pain during urination, drowsiness, dizziness and dry mouth, nose and throat.

2.2 Indirect risks (incorrect use): phenylephrine may adversely interact with other sympathomimetics, vasodilators and beta-blockers and other antihypertensives. The vasopressor effects of phenylephrine can be potentiated by digoxin, MAOIs, tricyclic antidepressants such as amitriptyline, amoxapine, clomipramine, desipramine and doxepin or tetracyclics such as maprotiline; antidepressants such as phenelzine, isocarboxylic acid, nialamide, tranylcypromine, moclobemide; Parkinson's disease drugs such as selegiline, and others such as furazolidone. Contraindicated for patients currently receiving or within 2 weeks of stopping therapy with MAOIs. Other medicines containing phenylephrine and ephedrine or other sympathomimetics such as those contained in local decongestants, e.g. nose drops. Decongestant nose drops should not be combined with combination products containing phenylephrine.

Paediatric population: frequency, type and severity of interactions in children over the age of 16 years are expected to be the same as in adults.

2.3 Recent cases at European level: -

3. CONCLUSIONS – RECOMMENDATIONS FOR LEGAL CLASSIFICATION

3.1 Member states' legal classification of the active ingredient for these therapeutic indications

(ATC codes) and supply conditions:

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

No more data available from other member states.

Melclass database[1]: Not subject to prescription.

3.2 Social dimension of classification:

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

Proposed recommendation: **List II + Exemption**

Exemptions: MS: 10 mg of phenylephrine; MDD: 40 mg of phenylephrine; short-term use.

Criteria: under the exemptions stated, the use of the product is considered to be safe; known use; self-assessment possible; medical advice to be sought if symptoms do not improve or worsen.

3.2.2 Paediatric use: Not recommended for children under 16 years of age without medical advice.

3.2.3 Social dimension: -

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

4. REFERENCES/COMMENTS

4.1 References: Martindale: The Complete Drug Reference - 37th Edition; databases of national competent authorities.

4.2 Comments: -

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