Notice

Regulatory cooperation initiative (RCI) over-the-counter (OTC) products

Release of final labelling standards

Health Canada and the Australian Therapeutic Goods Administration (TGA) have initiated the Regulatory Cooperation Initiative (RCI) project to explore various ways of work sharing between the two regulatory agencies. Two labelling standards have been developed (nonprescription topical nasal decongestants and nonprescription oral adult expectorant cough and cold) because they meet the goals of aligning the ongoing work of both regulators and reducing unnecessary differences.

The proposed nonprescription topical nasal decongestants labelling standard describes the requirements necessary to receive marketing authorization for non-prescription topical nasal decongestant products containing oxymetazoline hydrochloride or xylometazoline hydrochloride as a single ingredient for use in adults to relieve nasal congestion.

The proposed nonprescription oral adult expectorant cough and cold labelling standard describes the requirements necessary to receive marketing authorization for oral expectorant non-prescription products containing guaifenesin as a single ingredient for use in adults to relieve symptoms of common cold.

This initiative is the first of its kind between Health Canada and the TGA. This is one step in the ongoing collaboration between Health Canada and the TGA to work toward greater regulatory convergence and harmonization where feasible. Both regulators will continue to explore if there may be additional opportunities for future OTC monograph initiatives.
GUIDANCE DOCUMENT
Nonprescription topical nasal decongestants labelling standard

Published by authority of the
Minister of Health

<table>
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<tr>
<th>Date adopted</th>
<th>2014/03/10</th>
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<tbody>
<tr>
<td>Effective date</td>
<td>2014/05/30</td>
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Health Products and Food Branch
| Our mission is to help the people of Canada maintain and improve their health. | The Health Products and Food Branch's mandate is to take an integrated approach to the management of the risks and benefits to health related products and food by:
• minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food; and,
• promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their health. |
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<td>Health Canada</td>
<td>Health Products and Food Branch</td>
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Également disponible en français sous le titre : Ligne directrice : Norme d’étiquetage des médicaments décongestionnants nasaux topiques vendus sans ordonnance.
Foreword

Guidance documents are meant to provide assistance to industry and health care professionals on how to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent and effective.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document may be acceptable provided they are supported by adequate justification. Alternate approaches should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, in order to allow the Department to adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance documents.
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1. Introduction

This labelling standard describes the requirements necessary to receive market authorisation (Drug identification number (DIN)) for nonprescription topical nasal decongestant products containing oxymetazoline hydrochloride or xylometazoline hydrochloride as a single ingredient for use in adults and children 12 years of age and older to relieve nasal congestion. This labelling standard does not apply to products for use by children under 12 years of age.

2. Medicinal ingredients

Table 1: Drug medicinal ingredients

<table>
<thead>
<tr>
<th>Therapeutic class</th>
<th>Medicinal ingredient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decongestant</td>
<td>Oxymetazoline hydrochloride</td>
</tr>
<tr>
<td>Decongestant</td>
<td>Xylometazoline hydrochloride</td>
</tr>
</tbody>
</table>

3. Pharmaceutical forms

3.1 Acceptable

- Oxymetazoline hydrochloride as a nasal spray or as nasal drops.
- Xylometazoline hydrochloride as a nasal spray or as nasal drops.

3.2 Unacceptable

- oxymetazoline hydrochloride in a nasal jelly.
- xylometazoline hydrochloride in a nasal jelly.

4. Indications

4.1 Acceptable indications

- Temporary relief of sinus congestion and pressure due to colds or allergies.
- Helps clear nasal passages; Shrinks swollen membranes
- References to “runny nose”, "blocked nose", "stuffy nose" and “hayfever”.

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- References to “fast relief”, “Starts to work in minutes”, “Relief in minutes” or similar claims (AHFS Drug Information 2012, Martindale: The Complete Drug Reference, Parameters for the Diagnosis and Management of Sinusitis 1998).

- References to “long lasting”, “12 hour relief, or similar claims, for oxymetazoline hydrochloride. References to “long lasting”, “lasts up to 10 hours” or similar claims, for xylometazoline hydrochloride (Martindale: The Complete Drug Reference).

- Reference to “temporary” relief must be included once on the label in association with the label indications.

4.2 Unacceptable indications

The following indications for nasal decongestant products are excluded from the label and would require a review outside of the standard. Unacceptable indications include, but are not limited to:

- References to “sinusitis” (Parameters for the Diagnosis and Management of Sinusitis, 1998; American Academy of Pediatrics Subcommittee on Management of Sinusitis and Committee on Quality Improvement, 2001).

5. Dosage directions

5.1 Dosage for adults and children 12 years of age and older\(^1\)^\(^2\)

<table>
<thead>
<tr>
<th>Medicinal ingredient</th>
<th>Dosage strength</th>
<th>Recommended single dose</th>
<th>Dose interval</th>
<th>Maximum daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxymetazoline hydrochloride</td>
<td>0.05% w/v (0.5 mg/mL) nasal drops or spray</td>
<td>2 – 3 drops or sprays in each nostril</td>
<td>Every 10 – 12 hours.</td>
<td>2 applications in any 24 hour period.</td>
</tr>
<tr>
<td>Xylometazoline hydrochloride</td>
<td>0.1% w/v (1 mg/mL) nasal drops or spray</td>
<td>2 – 3 drops or 2 – 3 sprays in each nostril</td>
<td>Every 8 – 10 hours.</td>
<td>3 applications in any 24 hour period.</td>
</tr>
</tbody>
</table>

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\(^1\) First report of the expert advisory committee on nonprescription cough and cold remedies. Health and Welfare Canada, August 1988.

\(^2\) Handbook of Nonprescription Drugs An Interactive Approach to Self-Care seventeenth Edition 2012.
5.2 Dosing considerations

- Instruction to blow the nose before administering should be included.

Oxymetazoline hydrochloride 0.05% w/v (0.5 mg/mL) nasal spray or nasal drops - for metered spray volume should be approximately 50 - 100 µl per spray.

Xylometazoline hydrochloride 0.1% w/v (1 mg/mL) nasal spray or nasal drops - for metered spray volume should be approximately 50 - 100 µl.

6. Warnings

For outer and inner labels

The following directions/warnings are also required:

- Keep out of reach of children.
- Do not use for longer than three days
- Read the complete label [and package insert if applicable] prior to use and follow all label instructions.
- Do not use this product in children under 12 years of age.
- Frequent or prolonged use may cause nasal congestion to recur or worsen.

Further directions such as those in relation to use of the metered device or dropper and other safety statements, may be included as appropriate.

All of the following warnings may appear on a package insert or other panels if it can be demonstrated that space is limited on the packaging. Note that the packaging must carry clear instructions to access the insert or other panels:

- Do not combine with other decongestant products.
- Do not use more than the recommended dosage.
- Use of this container by more than one person may spread infection.
- Do not use if you have an allergy to any of the listed ingredients.
- If congestion persists, consult a doctor.
- May cause temporary discomfort such as burning, stinging, sneezing or an increase in nasal discharge (American Medical Association, 1980; Am. Soc. of Hospital Pharmacists,
Do not use if you have heart disease, high blood pressure, thyroid disease, diabetes, or difficulty urinating due to prostate enlargement, or if you are pregnant or nursing unless directed by a doctor.

- **In case of overdose:** Call a poison control centre or doctor immediately, even if you do not notice any signs or symptoms.

7. **Other labelling requirements**

For all products:

- **Declaration of ingredients:**
  - Single ingredient products and/or ones for which a compendial standard exists must declare the proper name of the finished product on the front panel of all labels, immediately preceding or following the brand name in a font size not less than ½ the size of the brand name. (C.01.004)
  
  - All products must declare the active ingredients on the inner and outer labels, and clearly label these as “active” or “medicinal” ingredients. (C.01.004)
  
  - Nonprescription products must provide a qualitative listing of “non-medicinal” ingredients on the outer label. (C.01.004)

- **Guidance document- Labelling of pharmaceutical drugs for human use:** This guidance document should be consulted for applicable labelling requirement.

- Acceptable other panels are **inner flap of cartons (if not glued) and inside panels of peel-back or accordion labels.**

**Legibility:**

Although no specific type size is mentioned in the Regulations, Section A.01.016 specifies that all information required to appear on a label must be:

- Clearly and prominently displayed, and
- Readily discernible to the purchaser or consumer under the customary conditions of purchase and use.
A person with normal vision, or those with corrective glasses that restore normal vision, should be able to read the information without straining. The colour, contrast, the position, and the spacing of the information are all to be taken into consideration in complying with these requirements.

8. **Specifications**

This labelling standard describes those requirements that are specific to this therapeutic class of drug.

Products must comply with the requirements in the *Food and Drugs Act* and associated *Regulations*. It is also noted that all products are subject to Part C, Division 2 of the *Food and Drug Regulations*.

All ingredient (medicinal and non-medicinal) and finished product specifications must meet or exceed the standards described in the publications referred to in Schedule B to the *Food and Drugs Act*, or equivalent standards. Where no Schedule B monograph exists for the dosage form, specifications should be similar to those of a comparable compendial dosage form. In the absence of a Schedule B standard for any dosage form, testing must be adequate to demonstrate the product's identity, potency, purity and quality.

Finished product specifications should include tests for identification and an assay with suitable limits for the medicinal ingredient(s). The specifications for all dosage forms should include a description of the dosage form, including organoleptic properties as well as physico-chemical testing e.g., pH, specific gravity, viscosity, appropriate to the dosage form. Where antimicrobial preservatives are added, an assay with suitable limits should be included. Antimicrobial preservative effectiveness should be determined in order to establish that the product is capable of resisting microbial contamination.

Any change to the manufacturing process that impacts the safety and efficacy of the ingredients, such as the use of novel technology (e.g. nanotechnology), requires supporting data and will be reviewed outside the labelling standard.

9. **Non-medicinal ingredients**

Non-medicinal ingredients must be restricted to those substances, necessary for the formulation of the dosage form. Their concentration must not exceed the minimum required to provide their intended effect. They must be harmless in the amounts used, their presence must not affect the therapeutic efficacy or safety of the medicinal ingredients and they must not interfere with assays and tests for the medicinal ingredients and, if present, antimicrobial preservatives. Sponsors should be aware that ingredients of botanical origin added as non-

10. References


