

05 May 2014

RASML Officer
OTC Medicines Evaluation
Office of Medicines Authorisation
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

Dear Sir/Madam,

Re: OTC nasal decongestant preparations for topical use - proposed advisory statements for labelling

Novartis Consumer Health (NCH) is the manufacturer and distributor of Otrivin® containing xylometazoline hydrochloride as the active ingredient.

We appreciate the opportunity to respond to the consultation on the proposed advisory statements for OTC nasal decongestant preparations for topical use. Our comments on the proposed Required Advisory Statements for Medicine Labels (RASML) are discussed below.

1. Proposed advisory statement: "Frequent or prolonged use may cause nasal congestion to recur or worsen."

NCH supports this advisory statement, as it provides clear information for consumers on why the medicine should not be used more frequently or longer than directed.

2. Proposed advisory statement: "Do not use for more than three days at a time unless advised by a doctor or pharmacist."

NCH proposes to amend this statement to "Do not use for more than ~~three~~ **five** days at a time unless advised by a doctor or pharmacist."

We agree that consumers need clear instructions on the maximum duration of use. However, the recommendation for 3 days is inconsistent with the body of clinical evidence and Australian standard reference texts.

Clinical evidence

Topical nasal decongestants are widely used to alleviate symptoms of rhinitis. These products are very effective at rapidly improving nasal congestion¹, a symptom which may in turn cause insomnia, snoring and disturbed sleep^{1,2}. Current evidence suggests prolonged or repeated use of topical decongestants can cause problems, leading to the development of rhinitis

medicamentosa (RM), commonly known as rebound congestion. This phenomenon becomes more frequent the longer the decongestant is used^{1,3,4,5,6}. It's understandable that when this occurs, patients become uncertain as to whether congestion is still being caused by the nasal disease or by RM. For this reason NCH agrees that there should be a statement on the packaging giving consumers clear instructions on the maximum duration of use. However, the timeframe of 3 days is inconsistent with the body of clinical evidence, and the mean duration of nasal symptoms experienced throughout the common cold; four to five days^{7,8,9}.

The rebound effect of topical decongestants has only been described experimentally in healthy subjects^{10,11,12,13}. Despite the fact that there are a similar number of studies in healthy subjects that failed to demonstrate any rebound effect^{14,15,16,17}, the results from these studies cannot be directly extrapolated to patients with rhinosinusitis. The nasal mucosa of healthy subjects is not subjected to the cytokine environment associated with inflammation. The inflamed nasal mucosa treated with a topical decongestant does not present the same absorption properties as healthy nasal mucosa¹. Evaluation of the congestion possibly induced by a topical nasal decongestant is consequently biased.

Randomised controlled trials conducted in subjects with inflammation of the nasal mucosa, show no signs of RM after treatment times of up to ten days. This is shown for studies conducted with xylometazoline^{18,19,20,21} and oxymetazoline^{22,23}. Subsequently, the majority of clinical reviews recommend limiting treatment time to ten days^{2,3,6,11,24}, with some cautiously recommending up to 7 days^{5,25,26,27}. Only one review had their lower limit of recommendation as 3 days⁵. The justification was not based on evidence but on the assumption that if a consumer was to choose to use it for longer, they still will be within a safe limit of use. However, supporting this rationale could encourage consumers to take a relaxed approach to medication labelling once they become aware directions for use can be extended.

Australian standard reference texts

Australian healthcare professionals frequently refer to the Therapeutic Guidelines, Australian Medicines Handbook (AMH), PSA's Non-prescription Medicines in the Pharmacy and Australian Pharmaceutical Formulary and Handbook (APF). In particular, the AMH and APF are standard texts required to be kept in pharmacies as per the Pharmacy Board practice standards and these are the references used by the majority of practicing pharmacists.

NCH notes that all the above references recommend a treatment duration of no more than 5 days, due to the risk of rebound congestion:

Australian Therapeutic Guidelines²⁸: *“maximum of 5 days”* for oxymetazoline, tramazoline and xylometazoline.

AMH²⁹: *“Do not use this medicine more than recommended or for more than 5 days at a time as it can worsen your symptoms when you stop using it.”*

PSA's Non-Prescription Medicines in the Pharmacy³⁰: *“Nasal decongestants should not be used for longer than 5 days at a time.”*

APF³¹: *“Topical decongestants should not be used for more than 5 days: prolonged use causes rebound congestion.”*

NCH believes that the proposed advisory statements should be aligned with the standard reference texts used by Australian healthcare professionals.

NCH recommendation

NCH proposes that the RASML advisory statements for topical nasal decongestant be amended as shown below:

Column 1 Substance(s)	Column 2 Conditions	Proposed for RASML Required statement(s)
Nasal decongestant preparations, including: <ul style="list-style-type: none">•Methoxamine•Naphazoline•Oxymetazoline•Phenylephrine•Tetrahydrozoline•Tramazoline•Tymazoline•Xylometazoline	When in nasal decongestant preparations for topical use	Do not use for more than five days at a time unless advised by a doctor or pharmacist.
		Frequent or prolonged use may cause nasal congestion to recur or worsen.

Thank you for your consideration of this response to the Consultation.

Regards,

Tra-My

Tra-My Nguyen
Regulatory Affairs Associate
Novartis Consumer Health Australasia
P.O. Box 4499
Mulgrave, Victoria 3170
AUSTRALIA



www.novartis.com

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