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| **Submissions to the Medicines Classification Committee for the Reclassification of** **Oxymetazoline Nasal Spray** **500mcg/ml** |
| **Present Classification:** Pharmacy-Only Medicine**Sought Classification:** General Sale Medicine |

**Date prepared:** 22July 2013

**Sponsor:** New Zealand Retailers Association (on behalf of Grocery Retailers)

**Applicant:** Pharmaceutical Solutions Ltd

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| Executive Summary |

Oxymetazoline is a selective alpha-1 agonist and partial alpha-2 agonist topical decongestant, used in the form of Oxymetazoline hydrochloride. It is a topical decongestant available as a nasal spray and used for temporary relief of nasal decongestion from colds, flu, hayfever and sinusitis.

Currently the treatment to alleviate general cold and flu with sinusitis symptoms available in the grocery channel is limited to oral formulations such as Phenylephrine. Products to relieve nasal discomfort and also relieve sinus congestion and pressure topically, such as anti-histamine or decongestive nasal sprays are currently only available through the pharmacies.

Oxymetazoline hydrochloride has been registered in New Zealand since 30 August 20011.

The current classification for oxymetazoline nasal spray is ‘Pharmacy Only’, except for nasal use when sold at an airport and/or for ophthalmic use when sold in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board.

The product is intended for short-term nasal administration for adults and children over 6 years of age, to clear blockages quickly by reducing nasal congestion.

The purpose of this application is to seek reclassification of oxymetazoline, when labelled for use in adults and children over 6 years of age, from ‘Pharmacy Only’ medicine to ‘General Sale’ medicine.

Oxymetazoline is available as ‘General Sale’ in UK3, Canada4 and USA; and as ‘Pharmacy Only’ in Australia7.

The intention of this reclassification is to provide the consumer with the convenience and choice of purchasing the nasal decongestant for the short term treatment to relieve nasal congestion from colds, flu, hayfever and sinusitis in an accessible environment which is not limited in hours of availability and/or location as it is at Pharmacy level. It is also an option for parents/caregivers who have pre-teen children who have difficulty breathing because of nasal blockages.

In addition, supermarkets generally open much longer hours than pharmacies18. Aside from those in malls, few pharmacies open on Sundays. Grocery stores are more prevalent in rural areas where there may be no other options for quick access to these medicines. The latest information sourced by the NZ Retailers Association still confirms that supermarkets opening hours are two times longer on average compared to pharmacies. This classification change enables access to consumers with after hour requirements.

Oral formulations of nasal decongestant containing phenylephrine such as Sudafed®, Dimetapp® and Maxiclear® are already available in the General Sale environment. By reclassification of oxymetazoline nasal spray to ‘General Sale’, it serves as an alternative dosage form option for patients with nasal decongestion. The proposed reclassification will incorporate indications and warnings consistent with the current nasal decongestant spray in the market for ‘Pharmacy Only’ medicine.

The safety and efficacy of oxymetazoline nasal spray has been reviewed extensively and the safety profile of oxymetazoline is well established. Side effects are also generally well tolerated. The proposed classification for oxymetazoline is not expected to increase the potential risk of adverse events nor the potential for abuse or misuse.

All Oxymetazoline nasal sprays currently listed on Medsafe (June 2013)1;

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| **Trade Name** | **Sponsor** | **Registration situation** |
| Dimetapp 12 Hour Nasal Spray Nasal spray solution, 0.5mg/mL (Pharmacy only) | Pfizer New Zealand Limited  | Consent givenApproval date: 30/08/2001 |
| Drixine Decongestant Nasal Spray Nasal spray solution, 500µg/mL (Pharmacy only) | Merck Sharp & Dohme (New Zealand) Limited | Consent givenApproval date: 14/05/2009 |
| Drixine No Drip Formula - Menthol Aroma Pump Mist Nasal Spray Nasal spray solution, 500µg/mL (Pharmacy only) | Merck Sharp & Dohme (New Zealand) Limited | Consent givenApproval date: 25/11/2010 |
| Drixine No Drip Formula - Moisturising Pump Mist Nasal Spray Nasal spray solution, 500µg/mL (Pharmacy only) | Merck Sharp & Dohme (New Zealand) Limited | Consent givenApproval date: 25/11/2010 |
| Drixine No Drip Formula Original Pump Mist Nasal Spray Nasal spray solution, 500µg/mL (Pharmacy only) | Merck Sharp & Dohme (New Zealand) Limited | Consent givenApproval date: 15/04/2010 |
| Sudafed Nasal Decongestant Nasal spray solution, 0.05%w/v (Pharmacy only) | Johnson & Johnson (New Zealand) Limited | Consent givenApproval date: 13/10/2011 |
| Sudafed Nasal Decongestant Spray Nasal spray solution, 0.5mg/mL (Pharmacy only) | Johnson & Johnson (New Zealand) Limited | Consent givenApproval date: 8/10/2009 |
| Vicks Sinex ExtraFresh nasal spray Nasal spray solution, 0.05%w/v (Pharmacy only) | Procter & Gamble Distributing New Zealand Limited | Consent givenApproval date: 1/07/2010 |
| Vicks Sinex Nasal Spray Nasal spray solution, 0.05%w/v (Pharmacy only) | Procter & Gamble Distributing New Zealand Limited | Consent givenApproval date: 1/07/2010 |
| Your Pharmacy Decongestant Nasal Spray Nasal spray solution, 0.5mg/mL (Pharmacy only) | Orion Laboratories (NZ) Ltd | Consent givenApproval date: 10/02/2011 |

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| Part A |

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| A.1. International Non-proprietary Name (or British Approved Name or US Adopted Name) of the medicine |

**Name:** Oxymetazoline

**Chemical structure:**

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**Molecular Formula:** [C](http://en.wikipedia.org/wiki/Carbon)16[H](http://en.wikipedia.org/wiki/Hydrogen)24[N](http://en.wikipedia.org/wiki/Nitrogen)2[O](http://en.wikipedia.org/wiki/Oxygen)

**Molecular Weight:** 260.375 g/mol

**CAS number:** 1491-59-4

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| A.2. Proprietary name(s) |

N/A

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| A.3. Name of company/organisation/individual requesting reclassification |

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| A.4. Dose form(s) and strength(s) for which a change is sought |

Our proposal is to reclassify oxymetazoline hydrochloride for nasal use, when labelled for use in adults and children over 6 years of age, from ‘Pharmacy Only’ medicine to ‘General Sale’ medicine.

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| A.5. Pack size and other qualifications |

This reclassification request is to permit the 20 ml nasal spray (500mcg/ml) to become a ‘General Sale’ medicine, when labelled for use in adults and children over 6 years of age.

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| A.6. Indications for which change is sought |

This proposal does not increase the range of indications or dosage recommendations for the use of oxymetazoline beyond those for existing nasal decongestant spray.

No change is sought in relation to indications. The current approved indications for oxymetazoline nasal spray in New Zealand are:

* Nasal decongestant spray helps relieve the nasal congestion of colds, flu, allergies, hayfever and sinusitis.

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| A.7. Present classification of medicine |

Currently in NZ, there is only 1 classification for Oxymetazoline and conditions are provided below

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| Classification2 | Conditions (if any) |
| Pharmacy Only | except for nasal use when sold at an airport;except for ophthalmic use when sold in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board |

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| A.8. Classification sought |

This application requests reclassification to ‘General Sale’ medicine status.

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| Classification | Conditions (if any) |
| General Sale | for nasal use in adults and children over 6 years of age when the strength is 0.05% or less |

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| A.9. Classification status in other countries (especially Australia, UK, USA, Canada)  |

Oxymetazoline Nasal Sprays are available as General Sale in UK**3**, Canada**4** and USA. It is classed as Schedule 2 medicines (Pharmacy medicine) available in the pharmacy over-the-counter in Australia. The conditions for General Sale in the UK and Canada are provided below.

| Country | Conditions (if any) |
| --- | --- |
| UK3 | Non-oily nasal sprays and nasal dropsFor use by adults and children over the age of 12 yearsMaximum strength: 0.05% |
| Canada4 | Nasal preparations for adult use and in ophthalmic products |

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| A.10. Extent of usage in New Zealand and elsewhere (e.g. sales volumes) and dates of original consent to distribute |

The nasal decongestant spray containing oxymetazoline hydrochloride 500mcg/mL has been registered and marketed in New Zealand since 2001.

Usage in New Zealand between 2008 to 23 June 2013:

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| --- | --- |
|   | New Zealand Pharmacy |
| Year 2008 | Year 2009 | Year 2010 | Year 2011 | Year 2012 | Cal YTD To 23/06/13 |
| Units (000s) | Sudafed Nasal Spray Pmp 18 | - | - | - | 14.8 | 13.2 | 4.2 |
|   | Sudafed Nasal Spray Pmp 20 | 0.0 | 0.0 | 11.5 | - | - | - |
|   | Drixine Reg Meter Pump 15ml | 14.2 | 15.2 | 14.3 | 1.2 | 0.0 | 0.0 |
|   | Drixine Reg Meter Refill 15ml | 22.1 | 18.6 | 20.4 | 7.5 | 1.2 | 0.1 |
|   | Drixine Reg Nasal Spry 15ml | 4.4 | 2.9 | 3.8 | - | - | - |
|   | Dimetapp 12hr Nasal Spray 20ml | 12.9 | 16.0 | 23.1 | 35.7 | 35.1 | 15.7 |
|   | Nasogel Nasal Spray 45ml | 0.1 | 0.7 | 0.4 | - | - | - |
|   | Vicks Sinex 12hr Nasal Spray 15ml | 13.3 | 2.6 | 0.0 | 0.1 | 0.0 | 0.0 |
|   | Vicks Sinex Pump Spray 15ml | 15.8 | 14.1 | 0.2 | 0.1 | 0.0 | 0.0 |
|   | Sinoclear Nasal Dcon Spray 135ml | 1.3 | 1.5 | 1.2 | 0.9 | 0.5 | 0.0 |
|   | Sinoclear Nasal Dcon Spray 25ml | 1.8 | 2.2 | 1.4 | 1.1 | 0.9 | 0.1 |
|   | Weleda Gencydo Nasal Spr 3% 20ml | 0.8 | 0.5 | 0.4 | 0.3 | 0.3 | 0.1 |
|   | Your Pharmacy Nasal Spray 20ml | - | - | - | 0.0 | 11.2 | 6.7 |
| Local Dollars (000) | Sudafed Nasal Spray Pmp 18 | - | - | - | 282.4 | 238.9 | 75.1 |
| Sudafed Nasal Spray Pmp 20 | 0.0 | 0.0 | 208.1 | - | - | - |
| Drixine Reg Meter Pump 15ml | 197.2 | 214.9 | 205.1 |   |   |   |
| Drixine Reg Meter Refill 15ml | 241.5 | 207.4 | 237.5 | 14.8 | 0.0 | 0.1 |
| Drixine Reg Nasal Spry 15ml | 54.7 | 35.8 | 48.7 | 98.8 | 15.9 | 1.4 |
| Dimetapp 12hr Nasal Spray 20ml | 186.5 | 241.8 | 367.2 | 576.9 | 562.5 | 257.8 |
| Nasogel Nasal Spray 45ml | - | - | - | 2.5 | 13.8 | 7.6 |
| Vicks Sinex 12hr Nasal Spray 15ml | 303.0 | 58.3 | 0.1 | 0.8 | 0.0 | 0.0 |
| Vicks Sinex Pump Spray 15ml | 181.7 | 166.3 | 2.8 | 0.7 | 0.0 | 0.0 |
| Sinoclear Nasal Dcon Spray 135ml | 25.0 | 30.6 | 24.0 | 21.2 | 10.8 | 0.3 |
| Sinoclear Nasal Dcon Spray 25ml | 21.5 | 27.7 | 18.6 | 17.0 | 12.9 | 2.1 |
| Weleda Gencydo Nasal Spr 3% 20ml | 16.1 | 9.9 | 10.4 | 8.2 | 8.6 | 3.1 |
| Your Pharmacy Nasal Spray 20ml | - | - | - | 0.0 | 152.1 | 99.8 |

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| A.11. Labelling or draft labelling for the proposed new presentation(s) |

Directions for use, indications and warning statements will remain the same as that for the current nasal spray products currently marketed in New Zealand, the only change being the removal of the ‘Pharmacy only medicine’ statement.

There is no requirement for different dosing instructions or indications for ‘General Sale’. It is important to ensure consistency of information so that consumers accustomed to using the product are not confused with conflicting information on packs bought in differing outlets.

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| A.12. Proposed warning statements if applicable |

The warning / precautions statements contained on the current labelling will remain the same. Typical precautions listed below.

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| PRECAUTION:* Continual use of this product for a period longer than 3 days in adults and 2 days in children is not recommended unless advised by a doctor.
* If congestion persists see your doctor or pharmacist.
* Ask your doctor before use if you are taking any other medicines to treat cough & cold.
* Ask your doctor before use in children aged 6 to 12 years.
* Do not use in children under 6 years old.
* Directions for use: For adults and children over 6 years of age: 1-3 sprays per nostril, 2-3 times a day when necessary. Maximum 6 sprays per day. Do not exceed recommended dosage.
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The above label warnings meet the labelling requirements stated in the Medsafe label statement database for nasal decongestants, which includes oxymetazoline6.

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| A.13. Other products containing the same active ingredient(s) and which would be affected by the proposed change |

There are currently 10 ‘Pharmacy Only’ oxymetazoline nasal spray products suitable for use in adults and children over 6 years of age registered in NZ and are listed below1:

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| --- | --- | --- | --- |
| Sponsor | Product1 | Pack sizes | Approval date |
| Johnson & Johnson (New Zealand) Limited | Sudafed Nasal Decongestant Nasal spray solution, 0.05%w/v | 18ml | 13/10/2011 |
| Sudafed Nasal Decongestant Spray Nasal spray solution, 0.5mg/mL | 20ml | 8/10/2009 |
| Pfizer New Zealand Limited | Dimetapp 12 Hour Nasal Spray Nasal spray solution, 0.5mg/mL (Pharmacy only) | 20ml | 30/08/2001 |
| Merck Sharp & Dohme (New Zealand) Limited | Drixine Decongestant Nasal Spray Nasal spray solution, 500µg/mL (Pharmacy only) | 15ml, 30ml | 14/05/2009 |
| Drixine No Drip Formula - Menthol Aroma Pump Mist Nasal Spray Nasal spray solution, 500µg/mL (Pharmacy only) | 15ml | 25/11/2010 |
| Drixine No Drip Formula - Moisturising Pump Mist Nasal Spray Nasal spray solution, 500µg/mL (Pharmacy only) | 15ml | 25/11/2010 |
| Drixine No Drip Formula Original Pump Mist Nasal Spray Nasal spray solution, 500µg/mL (Pharmacy only) | 15ml | 15/04/2010 |
| Procter & Gamble Distributing New Zealand Limited | Vicks Sinex ExtraFresh nasal spray Nasal spray solution, 0.05%w/v (Pharmacy only) | 15ml | 1/07/2010 |
| Vicks Sinex Nasal Spray Nasal spray solution, 0.05%w/v (Pharmacy only) | 15ml | 1/07/2010 |
| Orion Laboratories (NZ) Ltd | Your Pharmacy Decongestant Nasal Spray Nasal spray solution, 0.5mg/mL (Pharmacy only) | 20ml | 10/02/2011 |

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| Part B |

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| B.1. A statement of the benefits to both the consumer and to the public expected from the proposed change |

Oxymetazoline nasal spray has been available in NZ market for more than 10 years. Currently it is available for self-selection by patients in the pharmacy setting. It has been available at this level of classification for several years and no significant safety concerns have arisen5.

In Over-the-Counter (OTC) medications, oxymetazoline acts as a topical decongestant for temporary relief of nasal decongestion from colds, flu, hayfever and sinusitis.

Decongestant product available in the grocery channel is limited to oral formulations (e.g. tablets containing phenylephrine) and decongestive nasal sprays are currently only available through the pharmacies.

Pharmacy operating hours are generally short compared to operating hours of supermarkets. This can limit the access of consumers to required medication. A study in New Zealand by the NZ Retailers Association concluded that supermarkets were open for 101.5 hours per week on average and pharmacies were open 55.1 hours per week on average in the same areas examined8. The latest survey by the NZ Retailers Association still confirms that supermarkets opening hours are two times longer on average compared to pharmacies.

The reclassification of oxymetazoline nasal spray to a General Sale Medicine will allow consumers easier and more convenient access to an effective and safe short term therapy with after hour emergencies, especially in small towns throughout New Zealand which do not have a local pharmacy.

Directions for use on the pack include age and dosing guidelines to provide specific instruction for consumers to follow. Contact details for consumers wishing to seek additional product advice is also available on the pack.

There are sufficient warnings to alert consumers when not to use the nasal spray for their children and also when to seek medical attention e.g. before use, if the child has certain medical conditions or aged 6 to 12 years; and after use, to seek medical attention if congestion symptoms still persists.

This change will means that consumers in New Zealand will have the same access to oxymetazoline nasal spray as consumers in the United States, the United Kingdom and Canada.

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| B.2. Ease of self-diagnosis or diagnosis by a pharmacist for the condition indicated |

The indication for use and dose form proposed in this reclassification application for oxymetazoline nasal spray is essentially identical to those for nasal spray currently available as ‘Pharmacy Only’.

Nasal decongestant spray, containing 500mcg/ml of oxymetazoline is indicated for relief of nasal congestion from colds, flu, allergies, hayfever and sinusitis. All of these symptoms are well characterised, usually of limited duration, and easily identified and treated by a consumer who currently self-medicates with non-prescription medications.

The labelling directs consumers to seek medical advice and consult doctor or pharmacist before use if taking any other medicines to treat cough and cold and before use in children aged 6 to 12 years. The consumers are also advised to seek medical advice if the symptoms persist after 3 days. We believe that consumers recognize that prolonged pain/congestion is a sign of something more serious as such and are able to adequately evaluate this and seek appropriate medical treatment.

The labelling clearly states that the product is for short term use only, 1-2 sprays per nostril, 2-3 times a day when necessary for adults and children over 6 years of age, and maximum of 6 sprays per day.

The easily recognisable and short-term nature of the indications for use ensures that neither medical diagnosis nor on-going medical management are required.

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| B.3. Relevant comparative data for like compounds |

Topical and systemic sympathicomimetics have been used for many years to treat nasal congestion in diseases such as coryza and sinusitis. There are two groups of sympathicomimetics: the imidazoline derivatives (e.g xylometazoline, oxymetazoline) and the sympathicomimetic amines (e.g. pseudoephedrine, phenylephrine). Both are α-adrenoreceptor agonists. The imidazoline derivatives have a specific action on the α2-adrenic receptors while the sympathicomimetic amines act on the α1-adrenic receptors19.

Sympathomimetic amines and imidazole compounds are the most commonly used topical nasal decongestants11.

**Oxymetazoline VS Phenylephrine**

Phenylephrine is a selective [α1-adrenergic receptor](http://en.wikipedia.org/wiki/Alpha-1_adrenergic_receptor) [agonist](http://en.wikipedia.org/wiki/Agonist) used to relieve stuffiness that is associated with the common cold or allergy symptoms.

Prior to phenylephrine, pseudoephedrine was the common nasal decongestant which has been used for over 50 years in many over-the-counter formulations marketed as treatments for nasal congestion associated with colds, flu, hayfever and sinusitis. However, as [pseudoephedrine](http://en.wikipedia.org/wiki/Pseudoephedrine) is reported to have a greater incidence of central nervous system (CNS) stimulant effects than phenylephrine9, 10, phenylephrine is being marketed as a substitute for the decongestant [pseudoephedrine](http://en.wikipedia.org/wiki/Pseudoephedrine). Phenylephrine is now one of the most common OTC decongestants in the United States.

Both phenylephrine and oxymetazoline have in common that they are synthetic adrenergic agonists and stimulate α1 receptors of the ring like muscles surrounding blood vessels.

Phenylephrine belongs to a class of drugs called β-phenylethylamines which is sympathomimetic amines whereas oxymetazoline belongs to a class of drugs called Imidazolines with a longer duration of action than phenylephrine18.

A study that examined the effects of 2 common α-drenergic receptor agonists, oxymetazoline and phenylephrine, delivered in a nasal spray in a rabbit model evidenced ciliary loss, epithelial ulceration, inflammatory cell infiltration, secondary bacterial infection and, interestingly, cell vacuolization after 4 weeks of twice-daily administration12, 13. Phenylephrine 10% (491 mM, a formulation commonly used to induce mydriasis) has been shown to cause a reversible vacuolization of the corneal endothelial cells in rabbits and cats14 that was worsened when the corneal epithelium was damaged (extending to keratinocytes in this case)15. Adrenergic nasal decongestants have widely different durations of action18; for example xylometazoline and oxymetazoline are active for 10 h or more, whereas phenylephrine and naphazoline are typically active not more than 2–6 h16.

**Oxymetazoline VS Xylometazoline**

Oxymetazoline is closely related to xylometazoline hydrochloride both chemically and pharmacologically; both drugs are imidazoline derivatives.

A double-blind, placebo-controlled, parallel group study was performed21. 61 patients with a common cold were treated with xylometazoline 0.1% (29 patients) or placebo (saline solution; 32 patients; 1 spray three times a day for up to 10 days). The purpose of the study was to determine the decongestant effect (nasal conductance), the peak subjective effect (visual analog scale), duration of relief of nasal congestion, total and individual cold symptoms and general well-being (patients’ daily diary), and adverse events (AEs). In 2008, this study evidenced xylometazoline is an effective and well-tolerated decongestant nasal spray that significantly relieved nasal congestion compared with placebo in the common cold and provided long-lasting relief with just 1 spray, helping patients to breathe more easily for a longer period of time21.

There was a study performed to objectively determine and compare the decongestive effects of oxymetazoline and xylometazoline in healthy subjects20. The study population comprised 30 healthy adults. All subjects underwent active anterior rhinomanometry (AARhm) and acoustic rhinometry (AR) tests following the application of oxymetazoline, xylometazoline, or placebo (physiological saline). The change in nasal resistance, nasal airflow, and different cross-sectional areas (CSAs) of the nasal cavity in the subjects were examined for each solution separately20.

A total of 6,300 measurements of AARhm and AR were obtained. The application of placebo did not cause a statistically significant change in nasal resistance, nasal airflow, and CSAs (CSA1, 2, and 3, respectively) of the nasal cavity. In contrast, statistically significant changes in nasal resistance (inspiration p=0.000 and p= 0.004; expiration p=0.000 and p=0.000), nasal airflow (inspiration p= 0.000, and p= 0.004; expiration p=0.000 and p=0.000), and CSAs of the nasal cavity (CSA2 p=0.000 and p=0.000, CSA3 p=0.000 and p=0.00), with the exception of CSA1 (p= 0.982 and p=0.994), were obtained after the application of oxymetazoline and xylometazoline. A comparison of oxymetazoline and xylometazoline based on nasal resistance, nasal airflow, and CSAs of the nasal cavity demonstrated no statistically significant difference, except for CSA320.

The study concluded that oxymetazoline and xylometazoline are fast-acting and potent topical decongestants that have similar decongestive effects20.

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| B.4. Local data or special considerations relating to New Zealand |

It is not expected there would be any special considerations relating to New Zealand for this reclassification.

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| B.5. Interactions with other medicines |

Although drug interactions between oral dosage and topical nasal decongestants are not generally expected, they can occur. Oxymetazoline nasal spray can potentially interact with a number of other medicines (mostly prescribed medicine).

* Patients who have been prescribed certain monoamine oxidase (MAO) inhibitors, such as phenelzine, tranylcypromine or rasagiline, should not use products containing oxymetazoline hydrochloride. In addition, many antidepressants and blood control prescriptions can also react negatively with this medication.
* Patients with high blood pressure, diabetes, and thyroid disease are also advised against its usage.
* The safety of this medication in children and pregnant women has not been properly studied.

Persons using products containing this drug should carefully follow the labelled directions. The labelling for currently available nasal sprays in the market include adequate cautionary statements; to consult a doctor if you are taking any other medications to treat cough and cold.

For adults and children over 6 years of age, 1-2 sprays per nostril, 2-3 times a day with maximum 6 sprays per day. It is also advised not to use nasal sprays for more than 3 days in adults and 2 days in children unless advised by a doctor. Exceeding these dosage recommendations can drastically increase the potential for serious side effects.

However, short-term use of oxymetazoline nasal spray, at the recommended daily dose, is judged to have a low potential for interaction with other commonly administered pharmacological treatments5.

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| B.6. Contraindications |

The current labelling indicates the following contraindications/cautions:

* Do not use nasal spray in children under 6 years of age.
* Continual use of this product for a period longer than 3 days in adults and 2 days in children is not recommended unless advised by a doctor.
* Ask your doctor before use if you are taking any other medicines to treat cough & cold
* Ask your doctor before use in children aged 6 to 12 years.

These statements will remain on the label.

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| B.7. Possible resistance |

Not applicable as it is not expected that short term use of oxymetazoline will cause any resistance to develop.

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| B.8. Adverse events - nature, frequency etc |

Oxymetazoline has sympathomimetic properties. Toxicity studies in animals did not reveal any serious toxic effects when the drug was administered both topically and systemically17.

The oxymetazoline nasal spray has some side effects that occur only occasionally. For instance, it may cause:

* local stinging,
* burning,
* dizziness,
* dryness within the nose and/or throat
* headache,
* increase in nasal discharge,
* nausea,
* nervousness,
* sleep problems,
* sneezing

Effects of benzalkonium chloride

Benzalkonium is a common additive to oxymetazoline nasal sprays. Some studies have found that benzalkonium chloride may damage nasal epithelia and exacerbate rhinitis medicamentosa. However, the majority of studies find benzalkonium chloride to be a safe preservative22.

Use in pregnancy

The FDA has classified oxymetazoline nasal spray as a pregnancy Category C drug: Risk cannot be ruled out as human studies are lacking and animal studies are either positive for fetal risk or lacking as well. However, potential benefits may justify the potential risk.

However, neither oxymetazoline nor xylometazoline were found to be significantly associated with congenital malformations in two different studies23, 24, 25, 26.

Like all other medications they should be used only as directed during pregnancy. Use should be limited to 3 days as indicated on the packaging. Pregnant women should talk with their doctor/obstetrician before choosing an over the counter decongestant nasal spray.

Overdose

An overdose may be more likely to cause serious problems if it was taken by mouth, which might happen accidentally with a young child, rather than used as a nasal spray. Administration by parents can prevent the overdose.

The side effects mentioned above are more likely to occur in children because there is a greater chance in children that too much of this medicine may be absorbed into the body.

The labelling carries full information for the safe use of the product.

Below is the number of NZ cases for both adults and children reported to the Joint Adverse Event Notification System (JAEN) for the period from 01 January 2000 to 20 March 20135. JAENS contains information from reports of adverse events that the Therapeutic Goods Administration (TGA) and Centre for Adverse Reactions Monitoring (CARM) have received in relation to medicines used in Australia and New Zealand.

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| Number of reports/cases (NZ)Multiple adverse events have been reported for some patients | 2 |
| Number of cases with a single suspected medicine – Oxymetazoline Hydrochloride (NZ)(The TGA or CARM think there is a possibility that the medicine caused the adverse event) | 2 |

Given the above safety data and warning statements on the label, adverse effects with OTC short-term use oxymetazoline nasal spray are rare. Oxymetazoline should not be considered as just another decongestant but rather a safe, proven nasal decongestant spray which is internationally acknowledged for self-medication.

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| B.9. Potential for abuse or misuse |

Oxymetazoline nasal spray has been readily available in many countries for several years as an Over-the-Counter (OTC) product and has a very low to absent potential for abuse or misuse5.

The proposed reclassification of oxymetazoline nasal spray to a ‘General Sale’ medicine is not expected to increase the potential for abuse or misuse as this is for short-term emergency treatment only. It is also clearly stated on a pack to seek medical advice before giving to children aged 6 to 12 years and if taking any other medicines to treat cold and flu. Therefore reinforces informed use by consumers.

Oxymetazoline has no obvious potential for drug abuse. Serious central-nervous-system or blood-pressure effects have not been reported5. The potential for drug abuse with oxymetazoline nasal spray is therefore considered to be highly remote.

The key to further minimizing potential risks to the consumer is to continue to find better ways to educate (detailed information can be provided on product website), encourage consumers to read, comprehend and comply with current label warnings and directions for use.

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