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| **Submissions to the Medicines Classification Committee for the Reclassification of**  **TOPICAL MEPYRAMINE MALEATE 2%** |
| **Present Classification:** Pharmacy-Only Medicine  **Classification Sought:** General Sale Medicine |

**Date prepared:** 19 July 2013

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

**Applicant:** Pharmaceutical Solutions Ltd

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| Executive Summary |

Mepyramine, also known as pyrilamine, is a first generation antihistamine and has been available in the market since 1940s. It targets the Histamine-H1 receptors and is used to treat allergic reactions. As a topical cream it has local analgesic action to help ease the swelling and redness, and its antipruritic properties provides relief from the itch caused by allergic reactions.

Topical mepyramine is intended for short-term (few days) topical administration in adults, elderly and children to provide symptomatic relief of insect stings and bites, nettle rash and in some countries, jellyfish stings.

In New Zealand, topical mepyramine is currently classified ‘Pharmacy Only’ and this poses a limitation to consumers who require immediate access to the relief of skin allergic symptoms caused by insect bites, stings, and nettle rash.

The purpose of this application is to seek reclassification of topical mepyramine maleate from ‘Pharmacy Only’ to ‘General Sale’ medicine.

Topical mepyramine is classified as ‘General Sale’ in United Kingdom (UK), Canada and USA.

This reclassification application chose ANTHISAN Cream 2%w/w as the reference product as it is the only topical mepyramine registered in New Zealand. The proposed reclassification will incorporate indications and warnings consistent with that currently approved for Anthisan in the market as a ‘Pharmacy Only’ medicine.

The intention of this reclassification is to provide the consumer access to this rescue cream at a more convenient time and location. Due to the nature of the indication, it is most likely that consumers may need the medication during the weekends or off-peaks hours and possibly in remote areas where they are more prone to get insect bites and stings or nettle rash.

The wider location reach and operating hours of supermarkets are generally much longer than the operating hours of the general pharmacies. This classification change will enable consumer access to the medicine faster and easier. This is important as early application is essential to obtain the optimum response.

Pharmacy operating hours are generally short compared to operating hours of supermarkets. This can limit the access of consumers to the required medication. The reclassification of topical mepyramine to a ‘General Sale’ medicine will allow consumers easier and more convenient access to an effective and safe short term therapy. 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 same areas examined1. 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.

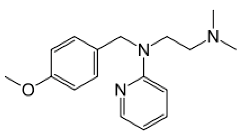
The safety and efficacy of topical mepyramine are well established and side effects are rare. As the indication is for relief from pain, itching and inflammation from insect bites, stings and nettle rash, this can be easily identified or self-diagnosed by the consumer. It is likely consumers will seek medical attention if their symptoms worsen therefore prolonged use of this product is not expected.

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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:** Mepyramine

**Chemical structure:**

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**Molecular Formula:** C17H23N3O

**Molecular Weight:** 285.38 g/mol

**CAS number:** 91-84-9, 59-33-6 (maleate)

**USAN:** Pyrilamine (United States Adopted Name)

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| A.2. Proprietary name(s) |

This reclassification application chose Anthisan as the reference product.

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| **Sponsor** | **Product**1 |
| Sanofi-Aventis New Zealand limited | Anthisan Topical cream, 2% |

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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 topical mepyrimine cream 2% 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 existing pack size of 25g to be a ‘General Sale’ medicine.

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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 topical mepyramine.

No change is sought in relation to indications. The current approved indication for topical mepyramine in New Zealand is:

Relief from pain, itching and inflammation from insect bites, stings and nettle rash.

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| A.7. Present classification of medicine |

Topical mepyramine is currently classified as a ‘Pharmacy Only’ medicine in New Zealand. The details are provided below:

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| **Classification**2 | **Conditions (if any)** |
| **Prescription** | except when specified elsewhere in this schedule |
| **Restricted** | For oral use in medicines for adults or children over 2 years of age other than in medicines used for the treatment of anxiety or insomnia; for oral use for the treatment of anxiety or insomnia when sold in the manufacturer's original pack containing not more than 10 dosage units |
| **Pharmacy Only** | For dermal use |

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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 dermal use. |

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

Topical mepyrimine is available as General Sale in UK3, Canada4 and USA5. The conditions for General Sale in the UK are provided below. In Australia6, topical mepyrimine is a Schedule 2, Pharmacy Medicine.

| **Country** | **Conditions (if any)** |
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| **UK**3 | External use  Max strength: 2%  For the symptomatic relief of insect stings and bites, nettle stings and jellyfish stings, in adults and children aged 2 years and over.    Max pack: 22g of the product  Additional product information requirements:  Repeated application to the same area of skin for longer than 3 days is not recommended. Do not use on cut, grazed or sunburnt skin or on large areas of skin. |

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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 |

Anthisan Topical Cream 2% has been registered in New Zealand since December 1969.

There is only one presentation of Anthisan Topical Cream registered and marketed in New Zealand:

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| **Sponsor** | **Product**1 | **Pack sizes** | **Approval date** |
| **Sanofi-Aventis New Zealand Limited** | Anthisan Topical Cream 2% | 25 g | 31/12/1969 |

The sales volume for Anthisan Topical Cream 2% for the last 3 years is an average of 75,000 units per year.

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

The product will be labelled with the same directions for use, indications and warning statements as the current Anthisan Topical Cream 2% registered in New Zealand. This is discussed further in Section A.12.

The ‘Pharmacy Medicine’ statement will be removed from the labelling.

There is no requirement for different instructions for use or indications for ‘General Sale’ medicine.

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| A.12. Proposed warning statements if applicable |

The product will be labelled with the same warning statement as the current Anthisan Topical Cream 2% registered in New Zealand. The warning statements are provided below:

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| **Contraindications**  Do not use Anthisan Cream if you have eczema or extensively broken skin.  **Warnings and Precautions**  Anthisan Cream should be applied directly to the site of the insect bite, sting or nettle rash 2-3 times a day for up to 3 days.  Discontinue use should skin sensitivity occur.  If symptoms persist, consult your doctor.  Prolonged use of greater than a few days is not recommended. |

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

There will be no other products affected by this proposed change.

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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 |

Mepyramine is classed as an antihistamine which helps relieve symptoms of allergic reactions. Used topically, it can relieve allergic skin symptoms such as reducing itchiness, swelling and redness.

Topical mepyramine is currently only available in pharmacies due to its ‘Pharmacy Only’ classification. But considering the nature of the indication of the product, it is more practical to make it more easily available since insect bites and stings, and nettle rash can happen at any time and anywhere.

Pharmacy operating hours are generally short compared to operating hours of supermarkets1 and most pharmacies are not open on Sundays. This can limit the access of consumers to the required medication. As grocery stores tend to be more prevalent in rural areas, consumers would benefit from the reclassification as it would mean faster access to the medication, which is essential to obtain the optimal response to topical mepyramine. The reclassification of topical mepyramine to a ‘General Sale’ medicine will allow consumers easier and more convenient access to an effective and safe short term therapy.

Additionally, if topical mepyramine is reclassified to ‘General Sale’, it would mean it would have a wider reach to more remote locations (where insect bites and stings are more likely to happen), as there may not be any pharmacies available.

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

The indication for Anthisan Topical Cream is symptomatic relief of insect bites and stings, and nettle rash.

The need for treatment is easily recognisable and allows for self-diagnosis by the consumer. There are clear instructions for use on the label and there are warnings to ensure that the consumer is aware when Anthisan Topical Cream is suitable for use and when it should be avoided. It has instructions to limit the use of Anthisan Topical Cream to three days and to seek medical attention if symptoms worsen or persist.

The ease of self-diagnosis and availability of important instructions and warnings on the label allows for the safe use of the cream without supervision of a pharmacist. The consumer will have faster access to the medicine to help relieve their symptoms quickly and to minimise distress caused by the bites/stings. This is important as early application is essential to obtain the optimum response.

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

There are currently no other like compounds thus comparative data is unavailable.

However, there are two other brands of product with similar indication available in the market which is Stingose Topical Gel and Spray and Soov Bite Gel.

Stingose Topical Spray and Gel contains the active ingredient Aluminium sulfate 20% and are classified ‘General Sale’ medicines. The active ingredient is an unscheduled ingredient in New Zealand. Stingose gel helps to minimise the pain, inflammation and itching associated with stings and bites of most insects and plants, including ants, bees, wasps, mosquitoes, sandflies, sea lice and nettles.

Soov Bite Gel contains the active ingredients Cetrimide 0.5% and Lidocaine hydrochloride 3%. Due to the concentration of lidocaine, Soov Bite Gel is classified as ‘Pharmacy Only’ medicine. Soov is a pain and itch relief gel with antiseptic for stings and Insect bites. The lidocaine helps to anesthetise the skin and stop the urge to scratch wher as cetrimide as an antiseptic to help prevent infection.

The safety of all three brands of products, Anthisan, Stingose and Soov Bite is well established and side effects are rare.

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

As New Zealand is a country where the residents enjoy nature and adventure, it is even more beneficial to have topical mepyramine reclassified as ‘General Sale’ to allow wider access to the medicine.

It is not expected there would be any special considerations relating to New Zealand for this reclassification when warning statements and instructions for use are clear and easy to follow.

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| B.5. Interactions with other medicines |

**There are no known interactions with other medicines.**

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| B.6. Contraindications |

Anthisan Topical Cream is contraindicated in individuals with eczematous conditions or on extensively broken skin surfaces.

There is no evidence of the safety of mepyramine maleate in human pregnancy, but it has been widely used for many years without apparent ill consequence. Absorption of a significant amount after topical application is unlikely when used as instructed by the label, nevertheless, Anthisan Topical Cream should not be used during pregnancy or lactation, unless considered essential.

The current label indicates the following contraindications/warning:

**Contraindications**

Do not use Anthisan Cream if you have eczema or extensively broken skin.

**Warnings and Precautions**

Anthisan Cream should be applied directly to the site of the insect bite, sting or nettle rash 2-3 times a day for up to 3 days.

Discontinue use should skin sensitivity occur.

If symptoms persist, consult your doctor. Prolonged use of greater than a few days is not recommended.

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| B.7. Possible resistance |

Not applicable for topical mepyramine.

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

When used in the recommended therapeutic doses appropriately, topical mepyramine is usually well tolerated and the adverse events are rare.

Skin sensitisations have been reported on rare occasions.

The Joint Adverse Event Notification System (JAEN) 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 Zealand8. Based on the information gathered from JAEN for the period from 01 January 2000 to 01 March 2013, there are no reported events for topical mepyramine.

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| B.9. Potential for abuse or misuse |

Due to the nature of the indication and product, it is unlikely that topical mepyramine will be abused or misused. In cases where the symptoms worsen or persist, more often than not the consumer will seek medical attention.

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| References |

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