

# **SUBMISSION FOR RECLASSIFICATION**

## **ACONITE** **(Aconitum napellus)**

**WELEDA NEW ZEALAND LTD.**

P.O. BOX 8132

HAVELOCK NORTH

## RATIONALE

### Preamble

The recent change in the classification of aconite and the recommendation to set an exemption from scheduling levels has occurred as a result of the move towards harmonisation with Australian schedules. The exemption level set has implications for some homoeopathic medicines that are on the market in New Zealand, that are produced differently to homoeopathic medicines on the market in Australia.

Our aim in this submission is:

- To clarify the classification and schedule exemption levels so that they can be clearly and objectively applied to anthroposophical and homoeopathic medicines.
- To propose classification and schedule exemption levels based on active principle concentration.
- To propose classification and schedule exemption levels that fairly reflect the actual risk of the medicine to the consumer.

To our knowledge, there have been no reports of adverse effects associated with anthroposophical or homoeopathic medicines containing aconite that have initiated this change.

### **Rationale 1: Classification of plant substances on active principles**

Classification that is based only on the plant name could severely disadvantage some homoeopathic medicines. We consider that the most effective means to classify plant substances is to base the classification criteria on the “active principle” (usually alkaloids) concentration of the plant, where possible.

This would avoid the major discrepancies in alkaloid concentration and toxicity that exist between medicines made from fresh or dry plant and different plant parts, especially homoeopathic medicines. (*Refer Appendix 2*)

It would also avoid the differences in alkaloid concentration that can occur as a result of different manufacturing and extraction processes used in the preparation of herbal substances. (*Refer Appendix 1, point 6*)

As can be seen from Appendix 2, a “homoeopathic potency” of a plant made following one homoeopathic pharmacopoeia would contain quite different levels of alkaloids and therefore different toxicity to the same “homoeopathic potency” of a plant produced following another pharmacopoeia.

- **Dry Plant:** The highest alkaloid concentration of aconite, mentioned, is a dry root total alkaloid concentration of 1.5%. (*Refer Appendix 1, point 3*)  
Aconite mother tincture made following the Homoeopathic Pharmacopoeia of the United States, although made from fresh plant contains the equivalent of 10% of the

dry plant material and is called a 1x (10%) potency. (Refer Appendix 2)

**This 1x (10% of dry plant) potency would contain a maximum of 0.15% alkaloids.**

- Fresh plant: Aconite mother tincture (50% fresh whole plant juice), made following the German Homoeopathic Pharmacopoeia, contains not less than 0.055% and not more than 0.075% of alkaloids, calculated as aconitine (Refer Appendix 1, point 4.).  
**A 1x (10% of the fresh plant juice) potency made from this mother tincture would contain a maximum of 0.015% alkaloids.**

As can be seen from the above two points, there is approximately a **ten fold** difference in the aconitine concentration of homoeopathic potencies originating from methods based either on a dry plant concentration or a fresh plant juice concentration.

Medsafe Precedents: Previous wording of the Medsafe classification of plants referred to the percentage strength of the alkaloids of the plant, eg. Aconite; alkaloids of and salts, except in medicines containing less than 0.02% of the alkaloids of Aconite.

Australian Precedents: Many of the classifications of herbs in the Australian Standard for the Uniform Scheduling of Drugs and Poisons refer to the percentage strength of the alkaloids of the plant, eg. Schedule 2 (Pharmacy Medicine) BELLADONNA, in preparations containing 0.25 per cent or less of the alkaloids of belladonna.

**We consider that classification of plant medicines based on the active principle concentration removes the “grey” areas inherent in the present system. It provides objective and clear limits to use when classifying products.**

## **Rationale 2: Reclassification**

We consider that the general application of a Prescription Only Medicine classification to product containing aconite up to the general schedule exemption level of 10 mg per litre or per kilogram is not substantiated by toxicity data. We propose that a lower classification be applied to product containing lower concentrations of the alkaloids of aconite.

The therapeutic dose range for hyoscyamine is 0.15 mg to 0.3 mg hyoscyamine (refer to the Hyoscyamus reclassification submission). This dose range appears to have been used in the setting of the classification levels for hyoscyamine, eg.:

Pharmacist Only Medicine: Hyoscyamine; in liquid form for oral use; in solid dose form containing more than **0.3 milligrams per dose** or more than 1 milligram per recommended daily dose

**We propose that the same approach be used with the classification of aconite.**

Toxic and therapeutic doses:

Fatal/Toxic dose: 2 mg is the lowest fatal dose of alkaloids (aconitine) mentioned. (Refer Appendix 1, points 7. and 8.)

Therapeutic dose of aconitine: Various doses are given (refer Appendix 1, points 8, 9, 10, and 11) – the one chosen to work with is the aconitine dose referenced from The Extra Pharmacopoeia, Martindale = 0.1 mg up to 0.3 mg aconitine. (refer Appendix 1, point 11.).

There is an 10 fold difference between the lowest fatal dose (2 mg) and the middle of the therapeutic dose range (0.2 mg).

Previous classifications of Aconite (refer Appendix 3.) were based on a concentration of the alkaloids of Aconite at 0.02%. This equates to 0.2 mg alkaloids per 1 mL dose.

Low concentration, homoeopathic medicines are commonly presented in liquid or powder form, therefore classification based on pack concentration is included.

Proposed reclassifications – refer Part A, Point 8.

POM: Aconite, **alkaloids of**; for oral use in liquid or powder form in a pack containing more than 0.2 milligrams; in solid dose form containing more than 0.2 milligrams per dose; except in medicines for external use containing 0.02% or less of the alkaloids of aconite.

PM: Aconite, **alkaloids of**; for oral use in liquid or powder form in a pack containing 0.2 milligrams or less; in solid dose form containing 0.2 milligrams or less per dose;  
Aconite, in preparations for external use containing 0.02% or less of the alkaloids of aconite.

The effect of this reclassification is that:

Liquid or powder oral preparations in a pack containing more than a single therapeutic dose of 0.2 mg of the alkaloids of aconite, and solid dose forms containing more than 0.2 mg per dose are classified as Prescription Only Medicines.

Liquid or powder oral preparations in a pack containing a single therapeutic dose of 0.2 mg or less of the alkaloids of aconite, and solid dose forms containing 0.2 mg or less per dose are classified as Pharmacy Medicines.

External preparations containing 0.02% or less of the alkaloids of aconite (usually a 1% to 2% aconite concentration depending on the alkaloid concentration of the root) are classified as Pharmacy Medicines.

This is in contrast to a previous NZ classification that placed this concentration of external preparation into a General Sale Medicine category.

(Refer Appendix 3.: General Sale Medicine: Aconite; alkaloids of and salts, in medicines for external use containing less than 0.02% of the alkaloids of Aconite.)

### **Rationale 3: Schedule exemption level based on active principle concentration**

#### The aim is:

To provide an exemption level for aconite based on the alkaloid concentration, not the plant name.

To provide an exemption level that is approximately equivalent in active principle concentration to the present Australian, and recommended NZ, schedule exemption of 10 mg per litre or kilogram for aconite.

To provide a 1000 fold difference between a therapeutic dose and the dose of a product containing the exemption level.

#### Alkaloid concentration of the **present** aconite schedule exemption level:

10 mg/L/kg (aconite 0.001%) at a dried root alkaloid concentration of 1.5% (*refer to Appendix 1, point 3.*) results in:

**150 micrograms per litre or kilogram (0.000015%) maximum alkaloids**

#### Proposed schedule exemption – refer Part A, Point 8.

Aconite, in preparations containing 150 micrograms per litre or per kilogram of the alkaloids of aconite (0.000015%)  
(*As the largest pack size in the market is 100 mL, there is an extra safety factor of ten*)

The proposed schedule exemption level, based on the alkaloids of aconite, provides an exemption level that is equivalent in active principle concentration to the present Australian and recommended NZ schedule exemption for aconite.

Therapeutic dose of aconitine: Various doses are given (refer Appendix 1, points 8, 9, 10, and 11) – the one chosen to work with is the aconitine dose referenced from The Extra Pharmacopoeia, Martindale = 0.1 mg up to 0.3 mg aconitine.  
(*refer Appendix 1, point 11.*)

A 1 mL oral dose of a product containing 0.000015% of the alkaloids of aconite would contain 0.00015 mg (0.15 microgram) alkaloids.

This is a **1000 fold** difference between the middle of the therapeutic dose range (0.15 mg) and the dose of a product containing the exemption level (0.00015 mg).

**We consider that this is an extremely wide safety margin.**

An exemption level based on the alkaloid concentration would prevent inequities occurring because of differences in alkaloid concentration of “homoeopathic potencies” made following different homoeopathic pharmacopoeia (*refer Appendix 2*).

#### As pointed out in Rationale 1.:

1x (10% of dry plant) potency would contain a maximum of 0.15% alkaloids  
1x (10% of the fresh plant juice) would contain a maximum of 0.015% alkaloids.

The present schedule exemption level of 10 mg/L/kg would result in:

- Aconite, dry plant 5x (0.001%) containing a maximum of 0.000015% alkaloids **being exempt from classification.**
- Aconite, fresh plant juice 4x (0.01%) containing a maximum of 0.000015% alkaloids **being classified.**

At present the exemption level would result in two products that contain the same level of alkaloids being differently classified, one being classified and the other exempt.

The proposed schedule exemption of the alkaloids of aconite at 0.2 mg/L/kg results in:

- Aconite, dry plant 5x (0.001%) containing a maximum of 0.000015% alkaloids **being exempt from classification.**
- Aconite, fresh plant juice 4x (0.01%) containing a maximum of 0.000015% alkaloids **being exempt from classification.**

This proposed exemption level would result in two products that contain the same level of alkaloids being both classified in the same way, i.e. exempt.

#### **Rationale 4: Safety in the market place**

Weleda medicines containing aconite have been on the market since the early 1950's and have had wide use during those years, in the customer base to which they are directed. There have been NO adverse reactions reported.

## PART A

**1. International Non-proprietary Name of the medicine**

Aconite

**2. Proprietary name(s)**

Non-specific change application for anthroposophical and homoeopathic products.

**3. Company requesting reclassification**

Weleda New Zealand Ltd.  
P.O. Box 8132  
Havelock North  
NEW ZEALAND

**4. Dose form(s) and strength(s)**

Not applicable.

**5. Pack size and other qualifications**

Not applicable.

**6. Indications for which change is sought**

Not applicable.

**7. Present classification of medicine**

Prescription Only Medicine: Aconite

Recommended general schedule exemption: 10 mg per litre or per kilogram

**8. Classification sought**

Prescription Only Medicine: Aconite, **alkaloids of**; for oral use in liquid or powder form in a pack containing more than 0.2 milligrams; in solid dose form containing more than 0.2 milligrams per dose; except in medicines for

external use containing 0.02% or less of the alkaloids of aconite.

Pharmacy Medicine: Aconite, **alkaloids of**; for oral use in liquid or powder form in a pack containing 0.2 milligrams or less; in solid dose form containing 0.2 milligrams or less per dose;  
Aconite, in preparations for external use containing 0.02% or less of the alkaloids of aconite.

Schedule exemption: Aconite, in preparations containing 150 micrograms per litre or per kilogram of the alkaloids of aconite (0.000015%)  
(As the largest pack size in the market is 100 mL, there is an extra safety factor of ten)

## 9. Classification status in other countries

Germany: *Prescription Only Medicine:* Aconite up to and including D3 (3x; 0.1%)

Australia: *Schedule 4 (Prescription Only Medicine):* Aconite (Aconitum spp)  
*Schedule exemption:* 10 mg per litre or per kilogram

## 10. Extent of usage in NZ and elsewhere

Homoeopathic preparations of Aconite are commonly used by homoeopaths and manufactured by most homoeopathic manufacturers.

## 11. Proposed labelling

Not applicable.

## 12. Proposed warning statements

Not applicable.

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

Anthroposophical and homoeopathic medicines.



## **PART B**

### **Reasons for Requesting Classification Change**

**1. Expected benefits to both the consumer and to the public**

Maintains accessibility to safe anthroposophical and homoeopathic medicines that have been used for minor, self-limiting conditions, in NZ for more than 40 years.

**2. Ease of self-diagnosis or diagnosis by a pharmacist**

Not applicable.

**3. Relevant comparative data for like compounds**

Not applicable

**4. Local data or special considerations relating to NZ**

Not applicable

**5. Interactions with other medicines**

None known.

**6. Contraindications**

Not applicable.

**7. Possible development of drug resistance**

None

**8. Adverse events**

Weleda medicines containing aconite have been on the NZ market since the early 1950's and on the European market since the early 1920's. During these years there have been, to our knowledge, no reports of any adverse events associated with these anthroposophical and homoeopathic medicines.

**9. Potential for abuse or misuse**

None

## Glossary, Appendices and Reference Copies

### Glossary

#### Anthroposophical medicine

The medicines specially made for anthroposophical therapy which contain herbal and homoeopathically produced preparations.

#### Homoeopathic medicine

Article 1 of the European Guidelines EG 92/73 and EG 92/74 on Homoeopathic Pharmaceuticals for Human respectively Veterinary Use provides the following definition [official within the 15 nations of the E.U.] of the term “homoeopathic medication”:

(1) ”Within the sense of this Guideline, a homoeopathic (veterinary) medication constitutes any medicinal agent, which has been prepared from products, substances, or compounds designated as homoeopathic source-material in accordance with homoeopathic manufacturing procedure as described in a European pharmacopoeia or – in absence of the corresponding monograph – according to the currently official pharmacopoeia of a member state.

(2) “Homoeopathic medication may contain multiple active constituents”  
[Official Journal of European Communities No. L 297/8 of Oct.13, 1992].

Homoeopathic medicines can be the mother tincture right through the range of homoeopathic potencies.

#### Homoeopathic potency

A homoeopathic potency is produced from one or several source material or mother tinctures, generally followed by potentising: serial dilution and succussion (potentisation). The following are examples of the common attenuation-ratios:

- 1:10 - Decimal or D, DH, or X potencies
- 1:100 - Centesimal or C, CH potencies
- 1:50,000 - Q or LM potencies

#### Potentisation

Potentisation: serial dilution and succussion - a special form of shaking the liquid dilution, or triturating the powder dilution.

#### Mother tincture

A mother tincture is a preparation of a substance, that is used as the starting material for the preparation of a homoeopathic potency, and in some cases can also be used as a homoeopathic medicine in its own right.

## Appendices

1. Appendix 1: References to Active Principle, Therapeutic and Toxicity Levels
2. Appendix 2: Concentration Differences Between Homoeopathic Medicines Using Aconite as an Example
3. Appendix 3: Previous Medsafe classifications of Aconite

## Reference Copies

1. Reference Copy 1: pg. 405-406, Pharmacognosy 14<sup>th</sup> Ed., by Trease and Evans, published by WB Saunders Company Ltd., ISBN 0-7020-1899-6
2. Reference Copy 2: Aconite Monograph date of issue: Feb.1993, The Lawrence Review of Natural Products – Monograph System, published by Fact and Comparisons, ISSN 0734-4961
3. Reference Copy 3: pg. 103, German Homoeopathic Pharmacopoeia (GHP) (Homoopathisches Arzneibuch HAB) Official Edition, published by Deutscher Apotheker Verlag Stuttgart Govi-Verlag GmbH, Frankfur, ISBN 0946717 05 2, ISBN for German original 3-7692-0932-X
4. Reference Copy 4: pg. 433, 434, Handbook of Poisoning, 12th Edition, published by Appleton & Lange, a Publishing Division of Prentice-Hall, ISBN 0-8385-3643-3
5. Reference Copy 5: pg. 303-304, Herbal Medicine, by Rudolf Fritz Weiss MD, English ISBN 0-906584-19-1, Translated from the Sixth German Edition of Lehrbuch der Phytotherapie, published by Hippokrates Verlag GmbH
6. Reference Copy 6: pg. 39, The Extra Pharmacopoeia, Martindale, Volume 1, 24<sup>th</sup> Edition, 1958, published by The Pharmaceutical Press