SUBMISSION FOR RECLASSIFICATION

HYOSCYAMUS NIGER

Request for reclassification of Hyoscyamus niger from pharmacy-only medicine classification to general sale medicine classification when the pack size contains 30 micrograms or less of total solanaceous alkaloids.

For the 29th MCC Meeting

WELEDA NEW ZEALAND LTD.

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HAVELOCK NORTH

RATIONALE

Preamble

This submission is to request the reclassification of Hyoscyamus niger from pharmacy-only medicine classification to general sale medicine classification when the pack size contains 30 micrograms (0.03mg) or less of total solanaceous alkaloids.

The original Weleda submission, to the 28th MCC meeting November 2002, requested a change to the level for exemption from scheduling.

> General Sale: Solanaceous alkaloids (eg. alkaloids of Belladonna and Hyoscyamus)
> - for oral use in packs containing 0.03mg or less of total solanaceous alkaloids.

This was addressed by the committee with the recommendation being:

- That the cut-off point for exemption from scheduling for atropine, hyoscine and hyoscyamine should be increased to 300 micrograms per litre or per kilogram.
- That the NDPSC should be recommended to adopt a similar cut-off point in Appendix G of the SUSDP

Weleda (New Zealand) Ltd does appreciate the fact that the committee accepted the submission and recommended a change to the cut-off point. However the change of wording from "packs containing 0.03mg " to "300 micrograms per litre or per kilogram " would result in a Weleda medicine, which contains 12 micrograms per 30mL pack size - 13.3 micrograms per maximum fill quantity of 33mL, being made pharmacy-only because it would contain 400 micrograms per litre.

We understand the need to harmonise with the wording in Appendix G of the SUSDP and therefore submit a request to reclassify Hyoscyamus niger in the pharmacy-only medicine classification section.

PART A

1. International Non-proprietary Name of the medicine

Hyoscyamus niger

2. Proprietary name(s)

Aurum 12x/Cardiodoron

3. Company requesting reclassification

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

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

Dose form: liquid

Strength: Aurum 12x/Cardiodoron

- Contains Hyoscyamus niger 0.2%, equivalent to 0.00004% total solanaceous alkaloids, equivalent to 12 micrograms alkaloids per 30mL pack size - 13.3 micrograms per maximum fill quantity of 33mL.

Dosage:

- A single dose of 15 drops is equivalent to 1mL.
- Dose: Take 5 drops (child under 7 years), 10 drops (7 to 14 years) or 15 drops (adult) 3 times daily at least 15 minutes before meals.
    - JETLAG: Take for up to 2 days before travelling and 7 days after travelling. Take up to every two hours while travelling (30mL is enough for 1 long or 2 short international flights).
    - SHIFTWORK: Take 3 times daily.

5. Pack size and other qualifications

Liquids: 30mL - maximum fill quantity = 33mL
glass bottles with tamper evident caps.

6. Indications for which change is sought

This anthroposophical medicine is indicated when daily rhythms are disturbed and upset sleeping patterns result, eg. jetlag, shiftwork.
We consider that these are minor and self-limiting conditions.

7. Present classification of medicine

Hyoscyamus niger

Pharmacy-only Medicine:
for oral use in liquid form in medicines containing 0.03% or less and 0.3 milligrams or less per dose and not more than 1.2 milligrams per recommended daily dose of total solanaceous alkaloids; in solid dose form in medicines containing 0.3 milligrams or less per dose form and not more than 1.2 milligrams per recommended daily dose of total solanaceous alkaloids

General Sale Medicine (as per recommendation from the 28th MCC meeting):
That the cut-off point for exemption from scheduling for atropine, hyoscine and hyoscyamine should be increased to 300 micrograms per litre or per kilogram.

8. Classification sought

Request for reclassification of Hyoscyamus niger from pharamcy-only medicine classification to general sale medicine classification when the pack size contains 30 micrograms or less of total solanaceous alkaloids.

Possible wording: Hyoscyamus niger

- Pharmacy-only Medicine:
- for oral use in liquid form in medicines containing 0.03% or less and 0.3 milligrams or less per dose and not more than 1.2 milligrams per recommended daily dose of total solanaceous alkaloids; in solid dose form in medicines containing 0.3 milligrams or less per dose form and not more than 1.2 milligrams per recommended daily dose of total solanaceous alkaloids;
- except when the pack size contains 30 micrograms or less of total solanaceous alkaloids.

Bold Lines: In the following table the MCC recommended cut-off point, 300 micrograms per litre or per kilogram, would operate at the point of the bold line in the table.

Hyoscyamus niger - strength of total alkaloids
Max. total alkaloids in fresh plant = 0.02% *(refer Appendix 1, point 12 in previous submission)*

Whole plant concentration	**Alkaloid concentration**	**mg total alkaloids/100mL**
100%	0.02%	NA
0.2%	0.00004%	400mcg/L
0.2%	**0.00004%**	**13.3mcg/33mL**
0.15%	0.00003%	300mcg/L

0.15%	0.00003%	9mcg/30mL
0.1%	0.00002%	200mcg/L
0.1%	0.00002%	6mcg/30mL

Double lines: In the following table the requested cut-off point in the pharmacy-only medicine classification, 30 micrograms per pack size, would operate at the point of the double lines in the table.

Whole plant concentration	**Alkaloid concentration**	**mg total alkaloids/100mL**
100%	0.02%	NA
0.2%	0.00004%	400mcg/L
0.2%	**0.00004%**	**13.3mcg/33mL**
0.15%	0.00003%	300mcg/L
0.15%	0.00003%	9mcg/30mL
0.1%	0.00002%	200mcg/L
0.1%	0.00002%	6mcg/30mL

The following concentration references have been used

- Fatal dose: 3mg has been used as the fatal dose, being somewhere between 1.6mg and 10mg atropine for a child. *(refer Appendix 1, point 13. and 14., refer previous submission)*
- Therapeutic dose: 0.3mg has been used as the therapeutic dose, being the dose referred to in the proposed pharmacy-only medicine classification as well as being in the dose range recommended by Martindale, being 0.15 mg to 0.3 mg. *(refer Appendix 1, points 15. to 20., refer previous submission)*

Substantiation for re-classification

- The MCC recommended cut-off point for exemption from scheduling of "300 micrograms per litre or per kilogram" would result in a 30mL pack containing 9 micrograms of total solanaceous alkaloids. The product in question contains a maximum of 13.3 micrograms of total solanaceous alkaloids.

- This submission is requesting an exemption from pharmacy-only classification for a "pack size containing 30mcg or less of total solanaceous alkaloids". Even though the product contains a maximum of 13.3 micrograms we have used 30 micrograms to keep within the principles of the herbal framework.

- A pack size of "30 micrograms or less of total solanaceous alkaloids" would contain approximately 1% (1/100$^{th)}$ or less of the fatal dose (3mg) (note that this fatal dose has an extra safety factor in that it is for a child not an adult); and

- the pack can contain only 10% (1/10th), or less, of a therapeutic dose. This ensures that no one could use a product with a general sale exemption in a conventional way. They would need to purchase 10 containers of product to achieve a conventional therapeutic dose.

- The product in this case contains a maximum of 13.3 micrograms per 33mL pack - 0.4 micrograms per 1mL dose, nearly 1/1000th of a conventional therapeutic dose of 300 micrograms.

- In conclusion we would suggest that if the pack size concentration is not delivering a conventional therapeutic dose, and if there is no risk from acute or chronic toxicity, then there are no safety issues and a general sale exemption should apply at the proposed concentration.

9. Classification status in other countries
Australia

SUSDP General Exemption: "any other substance included in Schedules 1 to 6, at a concentration not exceeding 10 mg per litre or 10 mg per kilogram, ……"

SUSDP Appendix G: general sale cut-off point for atropine, hyoscine and Hyoscyamine:

- Atropine = 100mcg per litre or kilogram
- Hyoscine = 10mcg per litre or kilogram
- Hyoscyamine = 10mcg per litre or kilogram

10. Extent of usage in NZ and elsewhere

This Weleda medicine has been available in New Zealand for over 40 years.

11. Proposed labelling

12. Proposed warning statements

If symptoms persist, consult your health care professional.
Keep all medicines out of reach of children

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

None

PART B

Reasons for Requesting Classification Change

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

The proposed exemption allows easy access, via health food shops and pharmacies, to a safe and affective product.
Disturbances arising from jetlag and shiftwork are common, self-limiting conditions, easily self-diagnosed and treated by the end consumer.
The proposed classification would allow the consumer to continue to easily access this safe, anthroposophical medicine that has been available in New Zealand for more than ?40 years.

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

Disturbances arising from jetlag and shiftwork are common, self-limiting conditions, easily self-diagnosed and treated by a pharmacist.

3. Relevant comparative data for like compounds

Not applicable

4. Local data or special considerations relating to NZ

None known.

5. Interactions with other medicines

None known.

6. Contraindications

None known.

7. Possible development of drug resistance

None known.

8. Adverse events

This Weleda medicine has been available in New Zealand for over 40 years.
During these years there has been, to our knowledge, no reports of any adverse events associated with this medicine.

9. Potential for abuse or misuse

We have no information that could indicate that there is any potential for abuse or misuse.

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.