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-Notice- Guidelines for the Use of Synephrine in Natural Health Products

January 2010

The Natural Health Products Directorate (NHPD) has conducted a review of the safety of synephrine, a substance which has structural resemblance to epinephrine and ephedrine.

Based on the potential for cardiovascular toxicity, the NHPD has adopted the following guidelines for the use of synephrine in Natural Health Products.

- A limit of 30 mg/day has been adopted as the maximum allowable dose for total synephrine and octopamine, which is related chemically and pharmacologically to synephrine. Sources of these substances include *Citrus* species such as *C. aurantium*, as well as certain species of some other genera (e.g. *Evodia rutaecarpa*), and synthetic sources. The above limit is consistent with that adopted by the Australian Therapeutic Goods Administration for synephrine in over-the-counter products (NDPSC 2003).
- Given that there is currently insufficient published clinical evidence to establish a safe level for synephrine + caffeine combinations, caffeine or caffeine sources (e.g. coffee, tea, cola, maté, guarana) will not be permitted in synephrine-containing products without submission of sufficient clinical evidence in humans.
- As there is insufficient information to establish the safety of long-term use of synephrine-containing products, a duration-of-use statement is required:
Consult a health care practitioner for use beyond 8 weeks (Greenway et al. 2006).

Risk Information:

- No risk information is required for products providing ≤ 3 mg synephrine + octopamine in a daily dose. This is based on a long history of safe use of bitter orange in Traditional Chinese Medicine at doses that provide approximately 3 mg/day synephrine.
- Risk information is required for those products providing >3 mg synephrine + octopamine in a total daily dose:

Cautions and warnings:

- Consult a health care practitioner prior to use if you have cardiovascular disease or hypertension (Sweetman 2007*; Haller et al. 2005; Bui et al. 2006), diabetes (Sweetman 2007*), prostate disorders (Sweetman 2007*) or are taking prescription medication (Sweetman 2007*; Genpharm 2005; Firenzuoli et al. 2005; Malhotra et al. 2001). Optional: prescription medications may be specified,



e.g. antihypertensives, thyroid hormones, Monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants.

- Consumption with caffeine-containing products (e.g. medications, guarana, maté, coffee, tea) is not recommended as it may increase the risk of adverse effects (Haller et al. 2005).
- Consult a health care practitioner prior to use if you are pregnant (Sweetman 2007*) or breastfeeding.

Contraindications:

- Do not consume if you are taking decongestant-containing cold preparations (i.e. phenylephrine or pseudoephedrine) (Penzak et al. 2001; NDPSC 2003), products containing ephedra or ephedrine (FDA 2004), or other medications which increase blood pressure.

* Based on risk information for sympathomimetics.

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