



Submission

Proposed changes to requirements for listed medicine ingredients: Annual low-negligible risk changes 2022-2023

Consultation paper

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BACKGROUND

About the NHAA

The NHAA is the peak professional association for the naturopathy and Western herbal medicine profession in Australia. Established in 1920, it is also the oldest professional association of complementary therapists in the country. The NHAA represents around 2,000 practitioners and is a member of the World Naturopathic Federation (WNF) which represents practitioners globally.

Our members provide primary care services to people suffering both acute and chronic disease. We use a combination of therapies, including diet, exercise, stress management, supplementation and herbal medicine formulations to deliver holistic treatments. We work alongside other health professionals to support conventional treatment. We play an important role in public health, including the quality use of medicines by Australian consumers.

The primary aims of the NHAA are to:

- Promote, protect and encourage the learning, knowledge and service delivery of naturopathic and Western herbal medicine
- Disseminate such knowledge through available media and networks
- Encourage the highest ideals of professional and ethical standards
- Promote naturopathic and Western herbal medicine as safe and effective public healthcare
- Engage with legislative tools and their representatives as they relate to the practice of naturopathic and Western herbal medicine in Australia

The vision of the NHAA is:

- Practitioners and the practice of naturopathic medicine and Western Herbal medicine are fully integrated into the primary healthcare system in Australia
- The NHAA is recognised as the peak body for naturopathic and Western Herbal medicine
- Naturopathic and Western Herbal medicine is accessible to all
- The integrity of the profession of naturopathic and Western Herbal medicine is maintained
- The standards and quality of education of the professions continue to be promoted
- Career opportunities and research pathways for naturopathic and Western Herbal medicine professionals are developed and maintained
- The integration of traditional knowledge and evolving science is continued

The NHAA publishes the quarterly *Australian Journal of Herbal & Naturopathic Medicine (AJHNM)*. The AJHNM publishes material on all aspects of medical herbalism and naturopathic practice including philosophy, phytochemistry, pharmacology and clinical application of medicinal plants. The NHAA also holds seminars throughout Australia, with the National Summit and Herbal and Naturopathic International Conference held on alternate years. Since its inception, the NHAA and its members have been at the forefront of naturopathic and Western Herbal medicine and have been influential in areas ranging from education and practice to ethics, regulatory and industry standards.

Proposed changes to requirements for listed medicine ingredients.

2. Liver injury associated with *Valeriana officinalis*

Proposed specific requirements:

The following warning statement is required on the medicine label when the medicine is for oral use: 'WARNING: Valerian may harm the liver in some people. If you experience yellowing of the skin/eyes, dark urine, nausea, vomiting, unusual tiredness, weakness, abdominal pain, and/or loss of appetite, stop using this product and see your doctor.'

Relevant rationale for the proposal is based on:

1. Between 1983 and 2021 (38 years) the TGA received 3 reports of liver injury in consumers taking products containing valerian as the only active ingredient, of which 2 cases were considered severe.
2. Internationally, 5 published cases in addition to 27 reports were located by the TGA with valerian as the single suspected medicine.
3. Details regarding preparation types, dose and duration of use were limited for many cases, with available information suggesting valerian associated liver injury is idiosyncratic with the mechanism of hepatotoxicity unknown.

Comments based on the evidence:

1. The root of *Valeriana officinalis* has been used since the time of Dioscorides and Galen and is a common and globally used herb today.
2. Internationally, expert opinion concludes there is no established link between consumption of valerian root and hepatotoxicity. These expert opinions come from the following monographs: European Medicines Agency¹ which includes an extensive overview of toxicological/safety data from clinical trials in humans, plus an assessment of adverse events, serious adverse events and deaths; Health Canada²; European Scientific Cooperative on Phytotherapy (ESCOP)³; and The Essential Guide to Herbal Safety⁴ -.
3. The US National Institutes of Health LiverTox publication provided a guidance note on *Valeriana officinalis* outcome and management that concluded "Hepatotoxicity from valerian is usually mild-to-moderate in severity and self-limiting. Only a small number of cases of liver injury attributed to valerian have been published, and there have been no instances of chronic hepatitis, cirrhosis or vanishing bile duct syndrome attributed to its use, and no convincing case of acute liver failure."⁵
4. The cited Kulkarni et al. abstract indicated there was no information on the name of the herbal tea or manufacturer, no information on what other products may have been in the 'valerian root based tea', no assessment for authenticity of product, potential contamination or adulteration, and no information on other herbs/supplements being taken concurrently. "[. . .] she admitted to using valerian root based herbal tea for anxiety. She was advised to discontinue this herbal tea which resulted [in] improvement of her aminotransferase levels."⁶
5. The cited Cohen et al. article provided no information on no authenticity assessment of the product, no assessment of contamination or adulteration. The authors note; "Given the lack of reported cases of this adverse effect, we feel that this reaction is quite rare."⁷The studies cited by the authors regarding cytochrome P450 3A4-mediated metabolism were based on *in vitro* or rodent studies⁷ which are not generalisable to human metabolism. Research on human volunteers shows that

- administration of valerian [root extract 125 mg, three times daily] had no significant effect on any CYP phenotypes [CYP1A2, CYP2D6, CYP2E1 and CYP3A4/5].⁸
- Systematic reviews indicate valerian is a safe herb with adverse effects that are mild and transient and no serious adverse events have been reported in clinical trials.^{9,10}

Whilst the NHAHA appreciates the risk assessment, the evidence is not substantial or conclusive enough to warrant a label warning. In the cited papers there is a lack of plant authentication, limited information on dosage variation and dose duration, no evidence of testing for adulteration, contamination or substitution, and a reliance on case reports. Compared to the widespread global use of valerian, with over 800,000 adults in the United States reporting use of valerian in the previous 30 days in 2012,¹¹ a label warning is considered unnecessary without proper expert procedural scientific assessment.

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