Australian Government
Department of Health, Disability and Ageing
Therapeutic Goods Administration

High-moderate risk changes to permissible ingredients – Proposal to remove *Andrographis paniculata* from the Permissible Ingredients Determination

Consultation outcome paper

Version 1.0, September 2026

Contents

Background

The ingredient '*Andrographis paniculata*' (Andrographis) is currently permitted for use in listed medicines and assessed listed medicines by way of its inclusion in the Therapeutic Goods (Permissible Ingredients) Determination (the Permissible Ingredients Determination).

The TGA first reviewed Andrographis following concerns about anaphylaxis in 2008, The TGA published a safety review and alert in 2015, with ongoing adverse event monitoring continuing thereafter. Since 2020, following High-moderate risk changes to permissible ingredients, all listed medicines containing Andrographis have been required to carry the following label warning about the risk of allergic reactions (including anaphylaxis):

> *'Andrographis may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis), stop use and seek immediate medical attention.*' (or words to that effect).

Following a large increase in the number of reports of anaphylaxis in 2019, the TGA has continued to receive a sustained high number of reports of anaphylaxis associated with Andrographis-containing medicines. A fatal case was reported in June 2024.

In April 2026, the TGA finalised and published an updated safety review with adverse event data to 31 December 2024, and a supplementary report with updated adverse event figures to 2025 evaluating the current evidence regarding the safety of Andrographis, the effectiveness of current risk-mitigation strategies, and regulatory options for further measures to address the risk. Current evidence regarding the safety of Andrographis considered in the updated safety review and supplementary report included expert advice from a clinical immunology and allergy specialist, advice from the Advisory Committee on Complementary Medicines (ACCM), adverse events in Australia and internationally, the formulations of the medicines involved in the Australian adverse events, available published literature since November 2011 and a toxicological review of non-clinical studies. The updated review and supplementary report concluded that Andrographis may not be appropriately positioned within the low-risk regulatory framework of listed medicines.

Consultation

The TGA invited stakeholders, including consumer associations, health professional associations including complementary medicine health professional associations, affected medicine sponsors and industry peak bodies, to provide feedback on the proposed removal of Andrographis from the Permissible Ingredients Determination under section 26BC of the *Therapeutic Goods Act 1989* (the Act). The targeted consultation commenced on 8 April 2026 and ended 8 May 2026.

All invited stakeholders were encouraged to refer to the published updated safety review and supplementary report prior to providing their submissions.

The proposed removal of Andrographis from the Permissible Ingredients Determination has been categorised as being of high-moderate risk, where a delay in changing an ingredient could cause serious or immediate harm.

The TGA received 29 submissions in response to the consultation:

- 13 were received from health professionals or health professional associations[1]. Of these:
  - 4 were from health professional associations outside of the complementary medicines sector
  - 6 were from health professional associations within the complementary medicines sector
  - 3 were from naturopaths
- 13 were received from affected sponsors and industry representative groups
- 2 were received from a consumer representative group and a consumer
- one was received from academia.

We acknowledge the disproportionate number of submissions from sponsors/industry/complementary medicine healthcare professionals in contrast to consumers and mainstream healthcare professionals.

Key themes of the submissions from health professional associations outside of the complementary medicines sector included:

- findings of the TGA safety review were broadly accepted
- findings regarding severity and unpredictability of anaphylaxis were acknowledged
- existing risk mitigation measures were viewed as ineffective
- public health and clinical burden were emphasised
- removal was strongly supported and agreement that the risk was considered incompatible with the listed medicines framework.

These respondents, who represent the healthcare sector outside of the complementary medicines sector, were broadly supportive of the TGA's proposal to remove Andrographis from the Permissible Ingredients Determination. These stakeholders were generally concerned about the risk to public health posed by the ingredient, including the severity and unpredictability of anaphylaxis and the clinical burden imposed on healthcare professionals and emergency services in managing adverse outcomes. These stakeholders were generally in agreement that the risk posed makes Andrographis unsuitable for inclusion in the listed medicines framework.

It is not possible to draw key themes from consumer representatives due to the low number of respondents (2); however, to summarise the views expressed:

- one respondent, identified as an individual consumer, was opposed to removal based on personal experience and comparison with other (mostly food) allergens
- the other respondent, a consumer representative group, was supportive of removal on precautionary public health grounds.

[1] A joint submission made by 3 health professional associations has been counted as a single submission.

One consumer representative cited concern about the frequency and severity of adverse event reports, particularly anaphylaxis. They acknowledged complexities in attributing causation in multi-ingredient products, but analyses in the TGA's safety review and supplementary report suggest that Andrographis is likely to be a significant contributing factor to the observed adverse reactions. From a public health and consumer safety perspective, they advocated for a precautionary regulatory approach where repeated associations with serious adverse events are observed, emphasising that removal is unlikely to negatively impact public health given the availability of alternative ingredients.

Key themes of the submissions from industry, complementary medicine health professionals/complementary medicine health professional associations, naturopaths and academia included:

- seriousness of anaphylaxis was generally acknowledged, but was regarded as rare/idiosyncratic in many of the industry submissions
- the TGA's interpretation of the evidence base was challenged by many of these stakeholders
- the risk was argued to be product-, formulation-, dose-, preparation- or patient-based rather than ingredient-intrinsic
- removal was considered by most to be disproportionate, premature and the most drastic option available
- preference was for the introduction of further risk-mitigating measures (such as stronger/more prominent label warnings, restrictions on co-formulation, education, dose/age/duration of use limits, restriction to practitioner-only access) followed by further evaluation.

Respondents representing industry, complementary medicine health professionals, complementary medicine health professional associations and academia were, almost unanimously, against the proposal with the exception of one that supported removal but considered access should be retained under practitioner only arrangements for appropriately trained herbal medicine practitioners.

Despite the submissions that did not support the removal of Andrographis from the Permissible Ingredients Determination, removal is still recommended. An analysis of the common themes presented by these stakeholders and reasons for why removal is still recommended follows.

Formulations, doses or ingredient combinations

A common position was that the risk may not be intrinsic to Andrographis as an ingredient, but instead be potentially linked to specific products, products from particular sponsors, extract types, excessive dose or particular combinations (in particular, co-formulation with Echinacea). Some respondents highlighted clustering of adverse events in particular products, and others suggested further stratified analysis by formulation type, extraction method, or ingredient combination should be considered before any blanket action is taken.

The available evidence does not support the view that the risk of anaphylaxis is confined to particular formulations, doses, extraction methods or co-formulation with

Echinacea. Consideration of formulation-related risk, including single-ingredient products, combination products and different preparation types, found that the weight of evidence supports that the risk relates to the ingredient Andrographis rather than being attributable to a particular formulation, with the relevant assessment set out across the formulation and risk profile sections of the safety review (p11-13 and 28-33[2]).

Although many adverse event reports involved products containing Echinacea, this association was considered in the context of supply data, which showed those products were supplied in much greater numbers. Overall, the proportion of anaphylaxis cases by formulation type broadly correlated with supply, and single-ingredient Andrographis products also showed disproportionate reporting of anaphylactic reactions and anaphylactic shock in international data (p24-27). Similarly, dose did not emerge as a reliable explanatory factor, as no clear trend was identified between andrographolide dose and anaphylactic adverse events, with reactions occurring across a wide dose range (p30-31). Further analyses and stratification by product type, extraction method, dose or ingredient combination is not recommended at this time given the existing data and the ongoing safety risk of severe allergic reaction including anaphylaxis. As acknowledged in the safety review, while the mechanism of reactions is not fully understood, and further research in this area may improve understanding of the allergenic mechanism behind Andrographis, the risk of life-threatening reaction is well-documented (p33-34). As such, it is recommended that Andrographis be removed from the Permissible Ingredients Determination on the basis of current evidence and the ongoing safety risk.

Further risk mitigation measures

Some respondents proposed alternative risk-management measures instead of removal. The alternatives commonly suggested included:

- stronger more prominent warning labels
- contraindications in people with allergies/asthma/previous reactions
- increased consumer/practitioner education
- enhanced pharmacovigilance
- practitioner only/pharmacist-supervised supply.

Alternative/additional risk-mitigation measures have been considered in the updated safety review, which concluded they were unlikely to adequately address the identified safety concern within the listed medicines framework. Strengthened warning statements and consumer education were assessed as unlikely to be effective because anaphylaxis associated with Andrographis is unpredictable, can occur rapidly, and often arises in individuals with no prior history of asthma, allergy or prior reaction. The safety review concluded that a warning about anaphylaxis is not expected to reduce its occurrence and noted that a voluntarily strengthened

[2] Page numbers relate to the published updated safety review, unless otherwise indicated as relating to the supplementary report, i.e. [supp].

front-of-pack warning introduced in 2024 had not reduced the number of anaphylaxis reports associated with this medicine (p38-41, p8-10 [supp]).

Suggestions for enhanced pharmacovigilance or further monitoring does not provide an appropriate alternative option while the risk remains, and fails to recognise pharmacovigilance processes to date, which have demonstrated a sustained pattern of serious adverse events without any clear lower-risk subgroup or modifiable factor that would support continued availability as a low-risk ingredient.

Proposals for practitioner-only or pharmacist-supervised supply are *not appropriate* risk mitigation measures within the listed medicines framework. These measures relate to scheduling and indicate that the respondents consider the ingredient unsuitable for self-selection and self-management. Where safe use depends entirely on professional oversight, this *supports* removal from the Permissible Ingredients Determination rather than retention within it. Of note, the product associated with the greatest number of anaphylaxis reports is subject to practitioner-only access imposed by the sponsor. This sponsor-imposed restriction has not been sufficient to mitigate the anaphylaxis risk related to that product.

Collectively, the risk controls proposed by respondents, including strengthened and more detailed label warnings, targeted contraindications, and supplementary information, are more consistent with the regulatory approaches applicable to registered medicines, where greater pre-market assessment and structured risk communication mechanisms are available.

Removal is disproportionate compared with risk management strategies employed for other products with allergy risks and with the actions of other international regulators

A recurring theme of submissions was that removal from the Permissible Ingredients Determination would be a disproportionate, premature, or an overly broad response to the identified risk. Many respondents argued that the issue was not whether the safety signal should be addressed, but whether full removal was justified.

Several respondents compared risk management approaches for allergy risks associated with foods or other medicines, including other listed medicine ingredients, and contended that risks for other substances are managed through labelling rather than prohibition.

The regulatory approach of label warnings for listed medicine ingredients such as royal jelly, propolis and pollen is noted. However, royal jelly risk management also includes compositional controls to address potential quality concerns, and it has not been established that label warnings alone mitigated its risks.

In contrast, for Andrographis, the label warning has not reduced reports of anaphylaxis, and no product quality issue has been identified as a contributing factor. In addition, other listed medicine ingredients associated with allergy or anaphylaxis do not show a comparable signal in Australian adverse event reporting, although they remain subject to ongoing monitoring.

As of June 2026, Andrographis is covered by monographs in the United States Pharmacopeial-National Formulary (USP-NF), British Pharmacopoeia (BP) and European Pharmacopoeia (Ph. Eur.), each specifying identification and other quality tests, with one also specifying an extraction ratio. Listed medicines containing Andrographis must comply with at least one relevant monograph, and sponsors must hold evidence demonstrating compliance with legislative quality and safety requirements. No information was provided to show that measures beyond these monograph requirements would improve the ingredient's safety profile, and the safety review found no compelling evidence that the issue was preparation-related (p31-33).

Comparisons with registered medicines such as non-steroidal anti-inflammatory drugs (NSAIDs) are not persuasive. Those medicines are regulated as registered medicines and undergo pre-market evaluation of safety, efficacy and benefit-risk balance before approval, unlike listed medicines.

Comparisons with foods and other regulated substances that are associated with anaphylactic risks are also of limited relevance because risk management approaches differ across regulatory frameworks. The incidence of anaphylaxis/allergic reactions to peanuts was not addressed in the review; however, peanuts and peanut oil are permitted for use in listed medicines. Medicine labels are required to declare the presence of peanuts or peanut products when used in medicines. Peanut allergy is one of the most common allergies in childhood, which can persist into adulthood, or develop in adulthood. Unlike Andrographis, a great deal is known about peanut allergy and factors that increase the risk of developing peanut allergy. Exposure through foods is far more likely than from a medicine – there are currently no listed medicines that contain peanuts, while very few contain peanut oil; and there have been no reports of anaphylaxis associated with peanuts in listed medicines received by the TGA to 8 April 2026.

In that context, the continued occurrence of severe anaphylaxis associated with Andrographis in listed medicines, including in first-time users and in individuals without a known allergy history, despite existing label warnings, indicates that the risk cannot be adequately managed through further labelling or other measures available within the listed medicines framework. The proposal for removal from the listed medicines framework is, therefore, considered proportionate and appropriate.

Differences in international regulatory practice, as raised by several respondents, are noted. However, direct comparison with Australia is limited due to differences in regulatory frameworks and reporting systems. Additionally, a current absence of regulatory action taken by other jurisdictions for some herbal ingredients may reflect the emergence of evidence over time. Accordingly, the absence of current comparable international regulatory action at this time does not indicate absence of a signal, nor an appropriate response to a safety signal in Australia.

Criticisms of the evidence/safety signal

A major theme was criticism of the data, methodology, and/or data interpretation in the safety review. Many respondents questioned whether the reported signal had

been adequately characterised, citing concerns such as lack of reliable denominators and uncertainty around incidence estimates, increased reporting following safety communications/media coverage, incomplete case information, conflation of suspected and confirmed anaphylaxis and insufficient product-level granularity.

No compelling evidence was provided to refute the conclusions of the review.

The criticisms raised about the evidence base do not materially alter the overall interpretation of the safety signal. While limitations such as the absence of robust exposure or usage denominators, incomplete case detail, and the inherent constraints of spontaneous adverse event data were acknowledged, these issues were already considered in the safety review and do not change the overall conclusion drawn from the evidence. Concerns about increased reporting following safety communications/media coverage also do not negate the signal. Sustained reporting of serious anaphylaxis has continued over time. Increased reporting following TGA or media activity may simply indicate that historical reporting levels are indicative of under-reporting rather than that the events were not occurring. Similarly, arguments about product-level clustering, insufficient granularity, lack of reliable incidence estimates, or the rarity and idiosyncratic nature of reactions do not overcome the broader findings of the review, which incorporated those limitations and still concluded that severe and unpredictable anaphylaxis remains associated with Andrographis. In that context, even though the data cannot show the exact frequency of reactions or fully explain the cause, the main concern remains the same: that the available evidence demonstrates an ongoing pattern of serious harm that is incompatible with the expectations for a low-risk listed medicine ingredient.

Potential consumer shift to unregulated markets

Many submissions argued that removal could move consumers away from Australian-regulated products and toward unregulated overseas or online supply, thereby potentially worsening safety outcomes.

The possibility that some consumers may seek unregulated overseas products does not negate the TGA’s responsibility to ensure products supplied within Australia meet appropriate safety, quality and efficacy standards and are positioned within the appropriate regulatory framework. Any risk of overseas purchasing is addressed through targeted enforcement, compliance activities and public awareness measures. Accepting the above argument would effectively create a “regulatory veto” whereby any proposed strengthening of standards or regulation could be opposed on the basis that some consumers may choose to take risks and circumvent the system. This would undermine the integrity of Australia’s therapeutic goods framework and role in safeguarding public health.

Other matters

Requested delay in regulatory action pending completion of proposed practitioner survey

One respondent proposed a practitioner survey to collect clinical data on Andrographis and requested a delay in regulatory action pending its completion. The survey is at a preliminary stage, lacks confirmed ethics approval and a defined timeframe, and is not expected to materially inform the established safety risk.

The safety review (p45) concludes that the risk of life-threatening anaphylaxis associated with Andrographis is not acceptable in the context of medicines indicated for low-level benefits. A delay to regulatory action in anticipation of further evidence is not considered appropriate for a well-documented life-threatening reaction associated with medicines currently regulated as low-risk products (p33).

The proposed survey may instead support a future application for registration, where products are individually evaluated for quality, safety and efficacy.

Criticism that the registered medicines pathway is not a practical alternative

One respondent submitted that the registered medicine pathway is not a practical alternative for Andrographis containing medicines because of the evidentiary and financial burden associated with registration, the uncertainty of approval, and competition from lower-cost overseas products. The respondent considers that removal of the ingredient from the listed medicines framework would, in practical terms, mean the loss of supply of Australian-regulated products.

A significant consideration for the Australian listed medicines framework is whether the risk-profile of an ingredient is compatible with the low-risk nature of framework. Rather than requiring individual TGA evaluation prior to market entry, listed medicines available for supply in Australia can only contain ingredients that are sufficiently low-risk and their entry on the Australian Register of Therapeutic Goods is reliant on sponsor certification, which includes safety for the purpose of use.

Sponsors of listed medicines are required to hold evidence supporting the quality, safety and efficacy of their products and, by listing a medicine, certify that they possess such evidence. Accordingly, sponsors seeking registration should already hold much of the underlying evidence necessary to substantiate their products. Registration requires that the evidence held by the sponsor be submitted to the TGA for product-specific evaluation. This enables the risks and benefits of a particular product to be independently assessed and, where appropriate, product-specific controls to be imposed.

The additional burden for sponsors of registered medicines arises from independent pre-market evaluation rather than sponsor self-certification. This is an appropriate safeguard where a medicine's risk profile is not compatible with the low-risk listed medicines framework.

Considerations relating to the commercial or economic viability of a particular regulatory pathway do not materially alter the assessment of whether an ingredient is

suitable for inclusion in a framework intended for lower-risk medicines. A primary consideration is whether the level of regulatory oversight applicable to that pathway is commensurate with the risks associated with the use of an ingredient.

Proposed changes to regulatory framework

One submission supported removal of the ingredient but proposed a staggered approach, including a practitioner-only access pathway to manage risks through qualified practitioner oversight by herbal medicine practitioners. As mentioned earlier, where safe use depends entirely on professional oversight, this supports removal from the Permissible Ingredients Determination rather than retention within it. The respondent also proposed broader structural reforms including statutory registration under the National Registration an Accreditation Scheme, which is under the remit of the Australian Health Practitioner Regulation Agency. The respondent also suggested activation of Schedule 1 of the current Poisons Standard to set out medicines that are access-restricted to naturopaths and western herbalists. These proposals relate to broader regulation of health practitioners, which is not within the remit of the TGA, and changes to the medicines regulatory framework. As such, the suggestion is outside the scope of this consultation.

Conclusion

Overall, following a thorough review and consideration of all matters, perspectives and evidence raised in the responses to the targeted consultation, the following evidence is presented that impacts the recommendation for the proposed amendment to the Permissible Ingredients Determination:

- Australian and international adverse event reports
- formulations of the medicines involved in the Australian adverse events
- available published literature since November 2011
- a toxicology review of non-clinical studies
- expert advice from a clinical immunology and allergy specialist, and
- expert advice from the ACCM.

The evidence evaluated by the TGA demonstrates that there continues to be a sustained and relatively high number of reports of life-threatening anaphylaxis associated with Andrographis, including a fatal case in 2024. The reactions are clinically serious, often occurring rapidly and requiring emergency treatment, and unpredictable – occurring both on first exposure and after prior tolerance, and frequently in individuals without a history of allergy. Risk may be elevated in the context of viral infections and concurrent use of NSAIDs. Although the true incidence cannot be precisely determined, available data suggest that anaphylaxis is expected to occur if supply of Andrographis-containing medicines in Australia continues at the same volumes as that analysed, with no evidence that specific formulations or preparation types can be considered lower risk.

Investigations did not identify risk mitigation strategies such as additional label warnings, formulation restrictions, or education that would sufficiently reduce the risk to support continued regulation as a low-risk listed medicine. The number and nature of reported adverse events in Australia are high relative to other oral medicines/ingredients associated with anaphylaxis, and international data demonstrates a sufficient safety signal to further support the need for regulatory action. Listed medicines are not subject to pre-market evaluation of efficacy or comprehensive risk-benefit assessment. Because they are intended to be safe for use without medical supervision and are self-selected by consumers, they have limited mechanisms for risk communication, such as information available on the label including warning statements, at the point of sale. In contrast, registered medicines, which have inherently higher risks, can include additional risk communication mechanisms such as patient leaflets, consumer medicine information, and health professional consultation where product information is available. In this context, the unpredictable and potentially fatal risk of anaphylaxis associated with Andrographis cannot be adequately mitigated and is not compatible with the low-risk regulatory framework.

There was no evidence or perspective presented in the consultation responses that alter the conclusions of the updated safety review that Andrographis presents a risk of life-threatening anaphylaxis that is inconsistent with the low-risk listed medicines regulatory framework. As such, it is recommended that an amendment be made to the Permissible Ingredients Determination to remove Andrographis.

Version history

Version	Description of change	Author	Effective date
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