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

Advisory Committee on Complementary Medicines

Minutes of Meeting 37

31 July 2025
Minutes ratified 5 November 2025

Abbreviations

ACCM	Advisory Committee on Complementary Medicines
AEMDS	Adverse Event & Medicine Defect Section
ARTG	Australian Register of Therapeutic Goods
BISS	Business Improvement and Support Section
CMES	Complementary Medicines Evaluation Section
COMB	Complementary & OTC Medicines Branch
FSANZ	Food Standards Australia New Zealand
IgE	Immunoglobulin E
L(A)	Assessed listed medicine
LCS	Listing Compliance Section
NHMRC	National Health and Medical Research Council
OTC	Over the Counter
PB	Pharmacovigilance Branch
TGA	Therapeutic Goods Administration

s22

Members of ACCM present via teleconference

Participant
s22
Specialist Advisor
s22

Participants from the TGA present

Participant	Role, Section, Branch
s22	

1. Administrative arrangements

1.1 Opening of meeting

The Chair opened the meeting at 9:30 am AEST, welcomed ACCM Members and TGA staff and offered a particular welcome to invited expert guest Professor s22 s22

1.2 Apologies

Nil.

1.3 Meeting declarations of interest

s22

1.4 Minutes of previous meeting

s22

2. Update on outcomes of previous issues considered by the ACCM

s22

s22

s22

s22

s22

3. Regulatory issues and updates

s22

s22

4. Advice items

4.1 *Andrographis paniculata* and anaphylaxis – Updated Safety Review 2025

The TGA's Adverse Event & Medicine Defect Section (AEMDS) within the Pharmacovigilance Branch is re-examining the safety of *Andrographis paniculata* (Andrographis) in listed medicines due to ongoing reports of anaphylaxis and other severe allergic reactions, including a fatal case in June 2024.

Previous regulatory actions included a 2015 safety advisory and review published in relation to Andrographis-containing listed medicines. Further, a mandatory label warning requirement about potential allergic reactions and anaphylaxis was introduced in December 2019, effectively mandating products released from 2 May 2020 to include the label warning.

An updated safety review was completed in July 2025 to assess the effectiveness of the current risk minimisation measures, and to reconsider these in the context of continuing reports of anaphylaxis. The review included:

- Expert clinical immunology and allergy specialist;
- Analysis of adverse event data (domestic and international);
- Review of medicine formulations involved in reported cases;
- Evaluation of published literature and toxicological data; and
- Consideration of international regulatory approaches

The review focused on assessing the effectiveness of current risk mitigation strategies and determining whether strengthened measures would adequately address the risk of anaphylaxis, given the availability of these products without medical oversight in the Listed Medicines framework.

ACCM discussion:

The topic was presented by three speakers. Comments from the speakers and the Committee have been summarised under the key concepts discussed.

- The first speaker, a TGA officer, presented findings from the TGA's updated safety review of Andrographis, highlighting ongoing high numbers of reports of

anaphylaxis despite existing mitigation measures. The review concluded that the unpredictable nature of the adverse events renders current risk mitigation measures inadequate, and that Andrographis appears to be inappropriately positioned in the regulatory framework as a Listed Medicine ingredient.

- The second speaker, an s22 , presented information supporting the unpredictable nature and severity of adverse reactions to Listed medicines containing Andrographis. The speaker discussed a case series of 17 patients treated over the past 12 months who experienced 23 serious reactions. s47G
- The presentation included an unpublished case series of 17 patients with clinical features of anaphylaxis associated with Andrographis exposure. s47G s47G s47G . There were seven first-time use reactions with no known prior exposure to Andrographis. Skin testing with crude tablet slurry of the product was performed in 6 cases and was negative for all. One patient with negative skin prick test was given a challenge with s47G s47G . Combined, these findings suggest the possibility of a non-Immunoglobulin E (IgE) based mechanism in some patients.
- The speaker spoke to mechanisms in anaphylaxis and noted contributing factors such as fever, virus and/or infection, nonsteroidal anti-inflammatory drugs (NSAIDs) co-administration, stress and alcohol intake. It was also noted that 8–10% of the Australian population may have hereditary alpha tryptasemia (HαT), which encodes alpha tryptase and is associated with increased risk and severity of anaphylaxis.
- The speaker noted that current label warning may be ineffective as many consumers do not read labels. Underreporting of adverse events was highlighted, attributed to patients not recognising symptoms as requiring medical attention, limited awareness among healthcare practitioners of patient supplement use, and lack of consumer knowledge on reporting mechanisms. The speaker acknowledged a significant safety signal and questioned the overall risk-benefit profile of Andrographis.
- The final speaker, an ACCM member, highlighted some of the limitations of the TGA's safety review, including the lack of pharmacovigilance data from high use areas in China and India. They also acknowledged that based on the characteristics of the case report details that standard risk mitigation strategies including label warnings and consumer awareness were unlikely to be sufficient risk mitigation strategies to prevent harm in all cases. They noted concerns particularly around combination formulas and concurred with the TGA that these concerns do not support Andrographis as a low-risk ingredient.
- The final speaker also referred to the conclusions of a systematic review and metanalysis (referred to by speaker 1) that concluded the evidence to support the efficacy and safety of *Andrographis paniculata* was of low quality and more research was required. This outcome was further contextualised by the speaker citing a paper that evaluated outcomes of a selection of 2428 (35%) Cochrane

Reviews. The evaluation found only 5.6% of the Cochrane reviews evaluating health interventions were supported by high quality evidence.

- The final speaker noted that Andrographis is documented in several pharmacopoeia, including the American, European, British, Ayurvedic, and Chinese, and noted the Chinese pharmacopoeia was the most detailed in terms of the number of compounds analysed.
- The committee expressed appreciation for the TGA's ongoing work and commitment to ensuring consumer safety. The complexity of the issue and the urgency of assessing potential risks to consumers was acknowledged by the committee.
- Queries, along with other key points that were discussed by committee members included:
    - Whether the safety signal is specific to Andrographis or potentially linked to combination products (e.g. when used with s47G s47G or other possible synergistic effects between ingredients.
    - There was discussion around the combination of Andrographis with s47G
    - There was discussion around the potential risks of using 2 herbal medicines in a combination product which traditionally would not have been combined.
    - While members agreed there was a clear signal for anaphylaxis from combination products, there was discussion that additional analysis of the data may assist to confirm the signal for Andrographis alone.
    - The committee suggested that the data presented in Table 7 of the updated safety review, which compared adverse event data for different medicines, should be reviewed and re-analysed as the Australian data was based on all Andrographis formulations including combination medicines while Australian data for other medicines appeared to be for single ingredient medicines.
    - Whether warnings or restrictions on combination products should be considered.
    - The role of formulation, extraction solvents, concentration/dose of certain constituents, and manufacturing practices in adverse events – uncertainty if, in contrast to traditional preparations, modern day formulations pose a higher risk due to different extraction methods and consequently, different constituent profiles and enrichments
    - The absence of pharmacovigilance data from countries with high Andrographis use, such as India and China.
    - The mechanisms attributing to the reaction, whether they are Immunoglobulin E (IgE)-mediated or an IgE-independent mechanism.
    - The potential involvement of contaminants, such as Aspergillus, which can cause severe allergic reactions in some people.
    - The need to investigate molecular analogues and metabolites.
    - The importance of understanding whether poor bioavailability or specific metabolites contributed to these adverse effects.
- The following summarises the TGA's consolidated response to the committee's queries and comments:
    - **Signal Strength and Specificity -** A strong and disproportionate safety signal has been identified for Andrographis as a standalone ingredient. As indicated in page 22 of Attachment 1 – Updated Safety Review 2025,

international adverse event data reveals a disproportionate increased reporting for anaphylactic shock (Information Component (IC) value of 2.1) for single ingredient Andrographis products. This signal is higher than that observed for single ingredient Echinacea purpurea products (IC 1.1) and even some Schedule 4 medicines associated with anaphylaxis. Anaphylaxis has been reported in association with single-ingredient Andrographis products in Australia, acknowledging that the number of reports received is proportionate to supply.s47G
s47G

- **Global Context -** The signal is supported by international pharmacovigilance data, particularly from Thailand. However, data from other regulators including India and China are not available, likely due to differing regulatory frameworks for herbal medicines which may not always be captured in pharmacovigilance systems.
- **Data Limitations -** The TGA acknowledged limitations in the data, including the inability to determine true usage rates from supply data, but noted that the current dataset represents the best available evidence.
- **Formulation and Manufacturing -** No consistent trends have been identified regarding specific manufacturers, concentrations, or formulations. All products are manufactured under GMP standards, and no manufacturer-specific signals have been detected.
- **Combination Products** – The Updated Safety Review 2025 specified that until December 2024, 254 anaphylaxis cases were reported. s47
s47
- The 2015 review identified Andrographis as the sole active ingredient in many cases, with a single active ingredient Andrographis medicine involved in the highest number of cases of any medicine at that time.
- The potential role of other ingredients remains an area of interest but has not been substantiated.
- **Mechanistic Considerations -** Questions regarding metabolism, specific metabolites, and molecular analogues fall outside the scope of the Listed Medicines regulatory framework.
- **Contaminants and Allergens -** No evidence has been found to suggest contamination (e.g., Aspergillus) as a contributing factor. Listed medicines are manufactured under GMP, and no manufacturer-specific signals have been detected.
- **Concentration/dose of certain constituents** – Although not further discussed in the meeting, the updated safety review included an analysis of data for andrographolide content and doses involved in anaphylaxis AEs. No trends could be identified to suggest reactions were related to andrographolide dose. The updated safety review also considered the constituent 14-deoxy-11,12-didehydroandrographolide which has a limit in place in the United States Pharmacopeia (USP) monograph for Powdered Andrographis Extract but not in the monographs for Andrographis or Powdered Andrographis. A brief literature search for review articles could not locate compelling evidence that 14-deoxy-11,12-

didehydroandrographolide is more likely than other constituents to cause anaphylaxis or other adverse events.

Discussion of the TGA's specific questions

1. **Whether the Committee agrees that, based on the available evidence, when Andrographis is used in listed medicines:**

    a. **there is increased risk posed to the consumer because the presence of viral illness can increase the likelihood or severity of an allergic reaction, and these products are mainly used for symptomatic treatment of viral illnesses.**

    b. **anaphylaxis adverse events have been sudden and unpredictable and therefore the risk of anaphylaxis is difficult to mitigate.**

    c. **further risk minimisation measures to strengthen label warnings, restrict formulations or publish further education are unlikely to mitigate the risk of anaphylaxis.**

    Whilst the committee unanimously agreed with all aspects of the above, one member expressed the view that the risk of the herb appeared to be significantly greater than the benefit. Other members noted that risks should be balanced against potential benefits and that traditional uses of Andrographis are broader than treating upper respiratory tract infections.

2. **Whether there is:**

    a. **any additional evidence that has not been considered by the TGA, or in the recent published literature that provides compelling evidence as to whether a specific preparation, use, dose, source of herbal material, or herbal constituent, is responsible for anaphylaxis observed with Andrographis.**

    b. **any other evidence pertaining to Andrographis and anaphylaxis that has not been considered by the TGA in this safety review.**

    The committee was unable to comment specifically on whether any additional evidence was available but highlighted several factors that need to be further explored before a decision can be reached on Andrographis as a single constituent.

    Several members highlighted that the safety data presented in the safety review suggest increased risk with combination products, particularly those containing Andrographis and Echinacea. Clearer analysis was recommended distinguishing products with Andrographis as sole active ingredient from those in combination with Echinacea.

    Another member considered that issues related to dose had not been completely addressed. Nevertheless, the member concurred that the risks still outweighed the benefits. Members highlighted that risk-benefit profile of Andrographis including implications for other traditional practitioners of utilising the herb should be considered.

    A member of the committee noted that modern extraction methods often produce highly concentrated and purified constituents, differing significantly from traditional use of Andrographis.

Several members were concerned about combination products of Andrographis with Echinacea, citing the evidence provided for adverse events especially when using combination products in the safety review and the lack of traditional precedent for their combined use.

A member also raised the possibility for Andrographis to be considered by the Scheduling committee for inclusion in the Poisons Standard.

ACCM advice and resolutions

ACCM advised the TGA Delegate of the Minister and Secretary that, in relation to each requested advice question:

1. **Whether the Committee agrees that, based on the available evidence, when Andrographis is used in listed medicines:**

    a. **there is increased risk posed to the consumer because the presence of viral illness can increase the likelihood or severity of an allergic reaction, and these products are mainly used for symptomatic treatment of viral illnesses.**

    Yes, the committee agrees.

    b. **anaphylaxis adverse events have been sudden and unpredictable and therefore the risk of anaphylaxis is difficult to mitigate.**

    Yes, the committee agrees.

    c. **further risk minimisation measures to strengthen label warnings, restrict formulations or publish further education are unlikely to mitigate the risk of anaphylaxis.**

    Yes, the committee agrees.

2. **Whether there is:**

    a. **any additional evidence that has not been considered by the TGA, or in the recent published literature that provides compelling evidence as to whether a specific preparation, use, dose, source of herbal material, or herbal constituent, is responsible for anaphylaxis observed with Andrographis.**

    b. **any other evidence pertaining to Andrographis and anaphylaxis that has not been considered by the TGA in this safety review.**

    The committee advised that while they could not provide any additional evidence, factors related to data analysis and an analysis of single ingredient Andrographis medicines vs combination products, as well as dose, preparation (modern extractions vs traditional use), risk/benefit, and the use of Andrographis in combination with other ingredients need to be given further consideration before the risk of Andrographis as a single listed ingredient can be clearly determined.

s22

s22