

From: [ADR Reports](#)
To: productsafety@blackmores.com.au; [S.22](#) [@blackmores.com.au](mailto: @blackmores.com.au)
Subject: Email from the TGA re Dear healthcare professional letter for Armaforce (AUST Ls 310158 and 340712) and risk of severe allergic reactions / anaphylaxis [SEC=OFFICIAL]
Date: Monday, 17 June 2024 2:38:06 PM

Dear [S.22](#),

Thanks for the phone discussion earlier today. As discussed we are considering risk mitigation options for the product Armaforce (AUST Ls 310158 and 340712) due to the number of serious allergic reactions reported for this product, including the recent case with a fatal outcome.

In a previous phone conversation on 11 June 2024 [S47G](#)

[REDACTED]

[REDACTED]

[REDACTED]

We consider that issuing a 'Dear healthcare professional' letter to increase the level of patient counsel at point of purchase is an additional risk mitigation option that may help to reduce the risk of severe allergic reactions. As the product is marketed as 'practitioner only' we consider this presents an opportunity to draw attention to the risk of anaphylaxis at the point of purchase, and to advise consumers to stop use if any reaction occurs, even mild.

You indicated in our phone call today that you have already done this by sending out an Armaforce prescribing reminder through your electronic direct mail (EDM) channel, which reaches all account holders who purchase the product. You confirmed that the product should only be available after consultation, therefore the EDM channel should reach all health care professionals who prescribe the product.

You stated that your prescribing reminder draws attention to dosing and adverse events, with anaphylaxis at the top of the list of known adverse events for this product. You also confirmed that the prescribing document reminds health care professionals to advise patients that if they experience allergic reactions they should stop use.

You agreed to send a copy of the prescribing reminder document. We will consider if it should be strengthened and/or distributed more broadly. We are aware that Armaforce is widely available at pharmacies and other retail outlets, and consider that all consumers who purchase this product should be made aware of the potential for anaphylaxis and severe allergic reactions at the point of purchase.

As mentioned in the phone call, we are continuing to follow-up the recent case and will keep you informed if we obtain further details. [S.22](#)

[REDACTED]

[REDACTED]

Kind regards,

[REDACTED]

[REDACTED]



Adverse Event & Medicine Defect Section
Pharmacovigilance Branch

Email: adr.reports@health.gov.au

Therapeutic Goods Administration
Australian Government, Department of Health and Aged Care
PO Box 100
Woden ACT 2606
www.tga.gov.au



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The Department of Health and Aged Care acknowledges First Nations peoples as the Traditional Owners of Country throughout Australia, and their continuing connection to land, sea and community. We pay our respects to them and their cultures, and to all Elders both past and present.



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From: [REDACTED]
To: [ADR Reports](#); [REDACTED]
Cc: [Product Safety](#)
Subject: RE: Therapeutic Goods Administration - Requests for Additional Information - ArmaForce (AUST L 340712) - [REDACTED]
Date: Wednesday, 19 June 2024 11:29:43 PM
Attachments: [image002.png](#)
[image008.png](#)
[image009.png](#)
[image010.png](#)
[Attachment 1. EDM v1 Armaforce prescribing reminder_070624.pdf](#)
[Attachment 2. Armaforce Prescribing Decision Tree.pdf](#)
[Attachment 3. EDM v2 Armaforce prescribing reminder_190624.pdf](#)
[Attachment 4. New warning added to websites_190624.docx](#)

Dear [s.22](#),

[REDACTED]
[REDACTED].

In accordance with our commitment to the appropriate prescribing of Armaforce and our proactive measures to reduce the risk of anaphylaxis, we have initiated the distribution of two electronic direct mails (EDMs) to reinforce the correct use of Armaforce. [s47G](#) [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

The first EDM, Version 1 (as detailed in Attachment 1 and 2), was circulated on Friday, 7th June 2024, [s.22](#) [REDACTED]

[REDACTED] we disseminated the second EDM, Version 2 (refer to Attachment 3 which includes the live link to Attachment 2), today, Wednesday 19th June 2024. This edition contains the new warning: "Do not use if you have a history of anaphylaxis."

Additionally, we have incorporated this new warning statement into the Armaforce product page, the campaign's landing page, and the Stock Keeping Unit (SKU) library featured on retailer websites (refer to Attachment 4).

We value your feedback on the prescribing reminder and the ongoing open dialogue we have maintained with you regarding this matter.

Regards,

[REDACTED]

[s.22](#) [REDACTED]



From: ADR Reports <ADR.Reports@health.gov.au>
Sent: Wednesday, June 19, 2024 11:52 AM
To: [s.22](#) [REDACTED] <[REDACTED]@blackmores.com.au>
Cc: Product Safety <productsafety@blackmores.com.au>
Subject: RE: Therapeutic Goods Administration - Requests for Additional Information - ArmaForce (AUST L 340712) - [REDACTED]

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Dear [REDACTED]

s.22

[REDACTED], can you please provide a copy of the 'Prescriber reminder' document you mentioned in the phone conversation on Monday 17 June 2024, also referred to in the TGA email of the same date (attached). Please provide this document by 5pm tomorrow (Thursday 20 June 2024).

Kind regards,

s.22

Adverse Event & Medicine Defect Section
Pharmacovigilance Branch

Email: adr.reports@health.gov.au

Therapeutic Goods Administration
Australian Government, Department of Health and Aged Care
PO Box 100
Woden ACT 2606
www.tga.gov.au

s.22

From: BioC Customer Service
Sent: Friday, 7 June 2024 2:59 PM
To: s.22
Subject: TEST | ArmaForce Prescribing Reminder

7th June 2024 | [View in Browser](#)



ArmaForce®

Dear Valued Customer,

Please be reminded of the prescribing information for ArmaForce®.

Prescribe ArmaForce® only as directed on the pack.

Directions for use:

Adults: Take 1 tablet once a day for a maximum of 2 weeks.

Label warnings:

- Andrographis may cause allergic reactions in some people.
- If you have a severe reaction (such as anaphylaxis) or develop any adverse symptoms stop use and seek immediate medical attention.
- Andrographis may cause taste disturbance including loss of taste, loss of appetite, vomiting and abdominal discomfort.
- Do not use during pregnancy or breastfeeding.
- Adults only.

Please advise your patient to stop taking the product at the first sign of any side-effects.

If consumers or their family members have experienced a suspected adverse event associated with our product, we encourage them to contact the BioCeuticals Naturopathic Advisory Team on 1300 650 455 or by email at advisory@bioceuticals.com.au.

To help determine when it might be appropriate to recommend ArmaForce®, download the **ArmaForce® Decision Tree**.

Yours in health,
Team BioCeuticals



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How to prescribe ArmaForce®

Document 2



Patient presenting with early symptoms of a common cold?

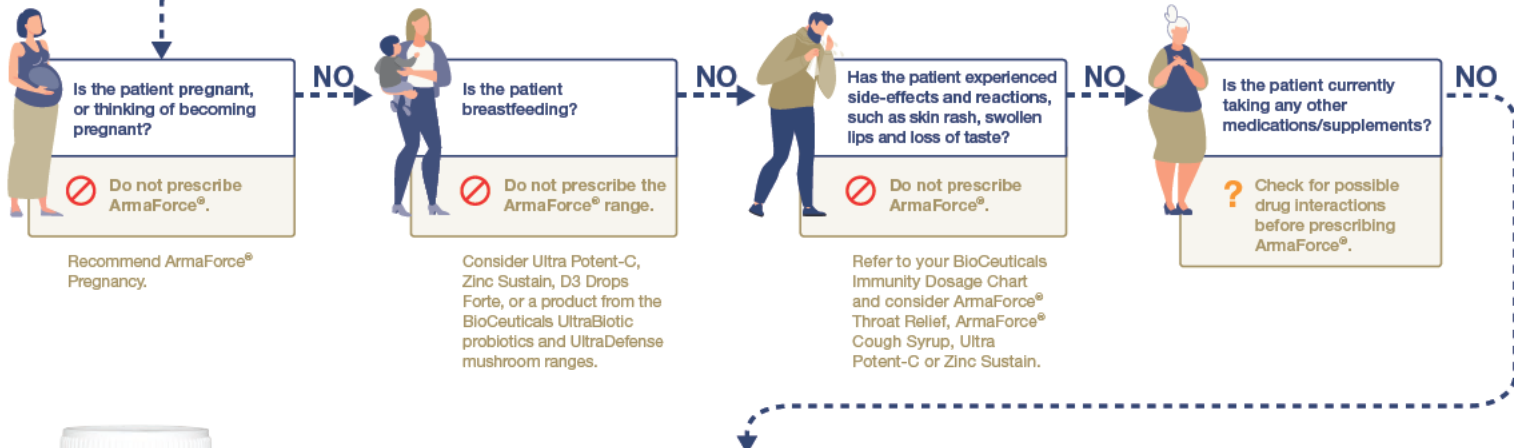
Patient wishing to purchase a complementary treatment to reduce common cold symptoms?

Patients wishing to support their immune system to fight illness?

Patient wishing to support their immune system and assist the symptomatic relief of common colds during the winter months?

Our hero and original formula ArmaForce® provides relief of symptoms of upper respiratory tract infections and common colds, assisting with sore throat and feverish conditions.

Please note our new dosage recommendation: **Adults: Take 1 tablet once a day for a maximum of 2 weeks.**
Before prescribing, please ask your patient the following:



? Did the patient answer "No" to all pre-prescribing questions?

✓ Prescribe ArmaForce® only as directed on the pack.

Advise your patient to stop taking the product at the first sign of any side-effects, and report directly to yourself, their qualified health professional.

Warnings on the product label

Do not use during pregnancy or breastfeeding. Andrographis may cause taste disturbance including loss of taste, loss of appetite, vomiting and abdominal discomfort. Andrographis may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis) or develop any adverse symptoms stop use and seek immediate medical attention. Adults only.



FOR PROFESSIONAL REFERENCE ONLY

s.22

Subject: FW: TEST | ArmaForce Prescribing Reminder

From: BioCeuticals <info@bioceuticals.com.au>

Sent: Wednesday, June 19, 2024 5:31 PM

To: s.22

Subject: TEST | ArmaForce Prescribing Reminder

19th June 2024 | [View in Browser](#)



ArmaForce®

Dear Valued Customer,

Please be reminded of the prescribing information for ArmaForce®.

Prescribe ArmaForce® only as directed on the product label.

Directions for use:

Adults: Take 1 tablet once a day for a maximum of 2 weeks.

Warnings:

- Do not use if you have a history of anaphylaxis.
- Andrographis may cause allergic reactions in some people.
- If you have a severe reaction (such as anaphylaxis) or develop any adverse symptoms stop use and seek immediate medical attention.
- Andrographis may cause taste disturbance including loss of taste, loss of appetite, vomiting and abdominal discomfort.
- Do not use during pregnancy or breastfeeding.
- Adults only.

Please advise your patient to stop taking the product at the first sign of any side-effects and seek medical attention.

If consumers or their family members have experienced a suspected adverse event associated with our product, we encourage them to contact the BioCeuticals Naturopathic Advisory Team on 1300 650 455 or by email at advisory@bioceuticals.com.au.

To help determine when it might be appropriate to recommend ArmaForce®, download the **ArmaForce® Decision Tree**.

Yours in health,
Team BioCeuticals



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New warning “Do not use if you have a history of anaphylaxis” added to the following:

1. ArmaForce Product Page:

s.22

Warnings:

- Do not use if you have a history of 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.
- Andrographis may cause taste disturbance, including loss of taste, loss of appetite, vomiting and abdominal discomfort.
- Do not use during pregnancy or breastfeeding.
- Adults only.
- Always read the label and follow the directions for use.
- If you have any pre-existing conditions, are on any medications, always talk to your health professional before use.
- If symptoms persist, talk to your health professional.
- Dietary supplements may only be of assistance if dietary intake is inadequate.
- Some products should be ceased at least two weeks before any elective surgery, please confirm with your health professional.
- KEEP OUT OF REACH OF CHILDREN.

2. ArmaForce Campaign Landing Page:

<https://www.bioceuticals.com.au/armaforce>

Take Daily	Take During	Take After
ArmaForce® Daily Protect Zinc, selenium and vitamins C and D to support a healthy immune system 2 tablets, once a day Wellmune® reduces duration of a common cold	ArmaForce® Reduces symptoms of common colds & flu Supports healthy immune system function Relieves fatigue Helps reduce free radical damage to body cells	ArmaForce® Recover 1 tablet, twice a day Siberian Ginseng aids in the recovery from illness and relieves fatigue Supports healthy stress response in the body Supports energy levels

Do not use ArmaForce if you have a history of anaphylaxis.
Always read the label and follow the directions for use.

3. SKU Library (Retailer sites)

From: s.22
To: ADR Reports;
Cc: Product Safety
Subject: INFORM: Urgent Implementation of Safety Measures for ArmaForce - Mitigating Anaphylaxis Risk
Date: Friday, 21 June 2024 8:46:58 PM
Attachments: image001.png
image003.png
image004.png
image005.png
Attachment 1. DRAFT Label WARNING OPTIONS BC ArmaForce (60) LAB V3.pdf

Dear ,

Thank you for the phone discussion on Wednesday, 19 June 2024. At Blackmores, the safety of our consumers is our utmost priority. Given the serious nature of anaphylaxis, we are compelled to take swift and decisive action to address this risk associated with ArmaForce.

Immediate Actions:

- **Stock on Hold:** s47G
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- **Packing of New Incoming Stock:** All packing of new incoming stock is currently on hold.

Further Initiatives:

- **Box Warning Addition:** To heighten awareness of the potential risk of anaphylaxis, we will add a new box warning to the ArmaForce product label, stating: “WARNING: Do not use if you have a history of anaphylaxis. Andrographis may cause anaphylaxis, which can be life-threatening. If swelling of the mouth, throat, or difficulty breathing occurs, seek immediate medical attention.”

s47G

- **EDM Messaging Revision:** Our Electronic Direct Mail (EDM) messaging will be revised to reflect the new box warning, further increasing prescriber awareness of the risk of anaphylaxis.
- **Product website and Prescribing Decision Tree:** We will update and add the new box warning to our Armaforce product page, the campaign’s landing page, the Stock Keeping Unit (SKU) library, and the prescribing decision tree.

s47G

- **SKU Specifics:**
 - ArmaForce 30’s
 - ArmaForce 60’s

- ArmaForce 120's
- **Stock Resumption:** We anticipate that stock for all SKUs will be available in trade from the end of July.

We are dedicated to maintaining the highest safety standards for our consumers s47G [REDACTED]. We seek TGA's guidance and approval on the box warning and the warning section on the draft label artwork (refer to attachment 1). We are open to and welcome any further recommendations from the TGA, and we intend to maintain an ongoing dialogue to refine these measures accordingly. We value TGA's prompt attention to this urgent matter and await your guidance.

Best regards,

s.22 [REDACTED]

s.22 [REDACTED]



From: s.22 [REDACTED]

Sent: Wednesday, June 19, 2024 11:30 PM

To: ADR Reports <ADR.Reports@health.gov.au>; [REDACTED]

[REDACTED]@health.gov.au>

Cc: Product Safety <productsafety@blackmores.com.au>

Subject: RE: Therapeutic Goods Administration - Requests for Additional Information - ArmaForce (AUST L 340712) - [REDACTED]

Duplicate email

[REDACTED]



From: [S.22](#)
To: [ADR Reports](#)
Cc: [Product Safety](#)
Subject: RE: INFORM: Urgent Implementation of Safety Measures for ArmaForce - Mitigating Anaphylaxis Risk [SEC=OFFICIAL]
Date: Friday, 28 June 2024 7:17:26 PM
Attachments: [image002.png](#)
[image008.png](#)
[image009.png](#)
[image010.png](#)
[Attachment 1. DRAFT Dear HCP letter Armaforce.docx](#)
[Attachment 2. DRAFT New Armaforce Prescribing Decision Tree.docx](#)
[Attachment 3. DRAFT WARNING FINAL BC ArmaForce \(60\) LAB V3.pdf](#)

Dear [S.22](#)

Thank you for TGA's review of Blackmores proposed safety measures for ArmaForce. We would like to update you on the actions we have already undertaken and the revised safety measures we are proposing.

Actions Already Undertaken:

- **Stock on Hold:** We have placed a hold on the current stock within our control of ArmaForce 30s, 60s, and 120s. [S.22](#)

Revised Safety Measures:

1. **Dear HCP Letter:** Enclosed is a draft of the Dear HCP letter (*attachment 1*). We would greatly appreciate the TGA's review and feedback. [s47G](#)
2. **Prescribing Tree Update:** Attached is a draft of the ArmaForce Prescribing Tree (*attachment 2*). We welcome the TGA's review and feedback. Upon finalisation, it will be linked to [s47G](#)
3. **New Label Warning Box for ArmaForce:** Please find the draft new label warning box (*attachment 3*), [s47G](#). We seek the TGA's review and feedback. The new label warning box will be applied to ArmaForce 30s, 60s, and 120s. [s47G](#)
All new labels will feature a TGA-aligned front-of-pack warning box, with no changes to the current back-of-pack warning (previously TGA approved).

4. [s47G](#)

5. **Website and Brand Updates:** The new warning box will be updated on the product website, SKU library, and the ArmaForce brand landing page.

s.22

We look forward to receiving the TGA's review and feedback on the revised safety measures outlined above. Should you require further information or clarification, please do not hesitate to contact me.

Regards,

s.22



From: ADR Reports <ADR.Reports@health.gov.au>

Sent: Thursday, June 27, 2024 9:54 AM

To: s.22 @blackmores.com.au>

Cc: Product Safety <productsafety@blackmores.com.au>

Subject: RE: INFORM: Urgent Implementation of Safety Measures for ArmaForce - Mitigating Anaphylaxis Risk [SEC=OFFICIAL]

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Dear s.22

Thank you for the proposed safety measures. We have reviewed your proposals and have some concerns which are detailed below. Also, please be aware that while we do not object to the addition of a prominent warning inside a box ('warning box'), we consider this to be an interim measure only. We are actively considering the suitability of the ingredient *Andrographis paniculata* in listed medicines. The outcome of our review may result in a different regulatory action. Any changes to regulatory requirements will be communicated following our usual processes, but to date we do not have a clear timeframe for this. Therefore, further changes may be required following our review, and we cannot confirm that your proposed interim measures are appropriate to mitigate the risks, particularly in the longer term.

We expect you are continuing to actively consider the benefit-risk balance for the medicines and whether they are safe for their intended purposes, as part of your sponsor obligations.

s47G

s47G

Labelling and product website

-

Wording of the proposed extended warning

Please ensure the wording is consistent with the current warning requirements for *Andrographis paniculata* (Andrographis) and includes all key elements of these. The allergy warning requirement includes instructions to stop use (or words to that effect). We note the proposed extended warning includes some elements of the current allergy warning requirement, while other elements are included in the usual 'Warnings' section. The dispersing of terminology and instructions across different warnings may not provide the intended message to consumers.

We consider the wording of your proposed extended warning does not use terminology that can be easily understood by most consumers. The current allergy warning requirement for Andrographis refers to 'allergic reactions' followed by 'if you have a severe reaction (such as anaphylaxis)'. The average consumer may not know if they experienced anaphylaxis but are likely to remember any severe allergic reactions. Further, different criteria can be applied to the diagnosis of anaphylactic reactions, which may or may not have been diagnosed as anaphylaxis depending on which criteria were used. Therefore please ensure the terminology is revised so that it is consistent with current requirements.

We also consider the proposed extended warning does not make it clear that it applies to previous reactions more broadly than to ArmaForce. You may wish to consider revising the extended warning to be clearer that it is referring to **any** history, not only to ArmaForce, if this is your intention.

Colour

We don't consider the proposed warning box is sufficiently prominent as it does not contrast with the usual colour scheme. The use of some red text and/or a red box and a white background inside the box would achieve greater prominence against the existing background colour.

Positioning

There is currently empty label space on the front label panel. Positioning the proposed warning box on the front label panel would achieve prominence and ensure the warning would be readily noticed by consumers at the point of purchase. This is particularly relevant for consumers who

have purchased and consumed the product in the past, who may not look at the rear panel. It would also be obvious to those who are selling the product, necessitating them to read the educational material to explain the warning to consumers.

GMP requirements for over-stickering and estimated time frame

s47G

This may affect your estimated time frames for implementation. Can you please provide an updated timeframe taking this into consideration, and also please advise if you intend to recall stock from the retail/trade level to apply the supplementary labelling.

Electronic Direct Mail (EDM) messaging, prescriber update and decision tree

EDM (Attachments 1 and 3 of your email dated 19 June 2024)

We consider that the updated EDM messaging does not make it clear that it contains important safety information. This could be achieved by using a clear subject heading that mentions safety, and providing an up-front safety statement at the top of the communication. There is currently nothing to alert recipients that an additional contraindication has been included nor the importance of this.

We also recommend that you consider including additional prescribing instructions to clarify the new contraindication 'Do not use if you have a history of anaphylaxis', if this is intended to apply to anaphylaxis and severe allergies to any substance.

This could include instructions to prescribers to always ask patients about any history of allergic reactions and anaphylaxis to any substance, and to advise patients not to use ArmaForce if they have ever experienced a severe allergic reaction or anaphylactic reaction to any substance, if this is the intention of the warning.

We also recommend you consider including instructions to:

- ask patients about any previous reaction to this product or to the ingredients Andrographis or *Echinacea* species (Echinacea), and to advise patients not to use ArmaForce if they have ever experienced any type of allergic reactions after taking any medicines containing Andrographis and/or Echinacea, as our adverse event data suggests subsequent reactions may be more severe.
- ask patients these questions regardless of previous use of ArmaForce.
- advise patients that some people develop anaphylaxis even after previously using the medicine without experiencing any adverse effects.
- advise patients to seek immediate medical attention at the first sign of a reaction, with particular emphasis on the following symptoms:
 - Difficult or noisy breathing
 - Swelling of tongue
 - Swelling or tightness in throat
 - Wheeze or persistent cough

- Difficulty talking or hoarse voice
- Persistent dizziness or collapse

Prescriber update and decision tree (Attachment 2 of your email dated 19 June 2024)

The decision tree includes the question 'Has the patient experienced side-effects and reactions, such as skin rash, swollen lips and loss of taste?' It is not clear if this is to ArmaForce or to any medicine or substance. This should be amended to provide further clarity that patients should not be prescribed ArmaForce if they have a history of severe allergy or anaphylaxis to any substance, if this is the intention behind the question. You should also consider asking about any previous allergic reaction to any products containing Andrographis or Echinacea and advise against use if yes.

We also recommend you consider including the additional prescribing instructions suggested above for the EDI communication in the bottom section of the prescribing document. The 'Warnings on the product label' section should also be amended to include the proposed warning box. This should be as it appears on the label (in the same prominent colours and style). I reiterate the above measures do not preclude further regulatory action and are considered voluntary interim measures that you have proposed to address immediate risk.

Please let me know if you have any questions, otherwise please provide a response to the concerns we have raised, as well as to the above questions about ArmaForce Day & Night, stock on hold, the level of implementation and an updated time frame for implementation as soon as possible but by no later than **5pm Friday 28 June 2024**.

Kind regards,

s.22

Adverse Event & Medicine Defect Section
Pharmacovigilance Branch

Email: adr.reports@health.gov.au

Therapeutic Goods Administration
Australian Government, Department of Health and Aged Care
PO Box 100
Woden ACT 2606
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The Department of Health and Aged Care acknowledges First Nations peoples as the Traditional Owners of Country throughout Australia, and their continuing connection to land, sea and community. We pay our respects to them and their cultures, and to all Elders both past and present.



Please consider the environment before printing this email.

Subject: Important Safety Information Regarding ArmaForce - Risk of Anaphylaxis

Dear Healthcare Professional (HCP),

Safety Statement: Please be advised that this letter contains critical safety information about the prescription of ArmaForce, particularly concerning the risk of anaphylaxis associated with Andrographis. It is imperative to adhere to the updated prescribing guidelines to ensure patient safety.

New Contraindication: Effective immediately, ArmaForce is contraindicated for use in individuals with any history of severe allergic reaction (anaphylaxis) to any substance. This precaution is based on recent adverse event reports and aims to ensure patient safety.

Prescribing Instructions: When considering ArmaForce for your patients, please:

1. **Inquire about any history of allergic reactions or anaphylaxis** to any substance, regardless of its relation to the ingredients in ArmaForce. Advise patients against using ArmaForce if they have ever experienced a severe allergic reaction or anaphylactic reaction to any substance.
2. **Specifically ask about previous reactions** to ArmaForce or its active ingredients, Andrographis and Echinacea species (Echinacea). If patients have had any type of allergic reactions after taking medicines containing these ingredients, they should not use ArmaForce.
3. **Pose these questions to all patients**, even if they have used ArmaForce previously without adverse effects. It is important to note that anaphylaxis can develop even after prior use without any reactions.
4. **Emphasize the urgency of seeking immediate medical attention** if patients experience any signs of a reaction. The following symptoms are particularly concerning and warrant prompt medical intervention:
 - Difficult or noisy breathing
 - Swelling of the tongue
 - Swelling or tightness in the throat
 - Wheeze or persistent cough
 - Difficulty talking or a hoarse voice
 - Persistent dizziness or collapse

Patient Education: Please ensure that patients are fully informed about the contraindications associated with ArmaForce and understand the importance of immediate medical attention if symptoms of anaphylaxis occur.

Product Supply: The product label will be updated with an additional and more prominent anaphylaxis warning. This will be applied across ArmaForce 30s (s47G), 60s (s47G) and 120s (s47G). This means that these products will be temporarily OOS until approximately mid-August.

Thank you for your attention to this important safety information. Your cooperation is essential in maintaining the well-being of your patients.

Sincerely,

[Name]

[Title]

[Contact Information]

ArmaForce® Prescribing Decision Tree with updated label warning.**WARNINGS:**

Allergic Reactions: Some individuals may experience allergic reactions to Andrographis. In the event of a severe reaction such as anaphylaxis, or if any adverse symptoms develop, discontinue use immediately and seek medical attention.

Severe Allergic Reaction History: Do not use ArmaForce if you have a history of severe allergic reactions. Andrographis may cause anaphylaxis. If symptoms such as swelling of the mouth or throat, or difficulty breathing occur, stop use and seek immediate medical attention.

Taste Disturbance: Andrographis may cause taste disturbances, including loss of taste, loss of appetite.

Gastrointestinal: Andrographis may cause vomiting and abdominal discomfort.

Adults Only: ArmaForce is intended for use by adults only.

Pregnancy/Breastfeeding Contraindication: Do not use ArmaForce if pregnant or breastfeeding.

1. Patient Eligibility

- Is the patient an adult and not pregnant or breastfeeding?
- ****No**** → Do not prescribe ArmaForce. Consider a suitable alternative.
- ****Yes**** → Proceed to step 2.

2. Allergy and Anaphylaxis History

- Has the patient ever had a severe allergic reaction or anaphylaxis?
- ****Yes**** → Do not prescribe ArmaForce. Consider a suitable alternative.
- ****No**** → Proceed to step 3.

3. Previous Reactions to Andrographis or Echinacea

- Has the patient previously reacted to Andrographis or Echinacea?
- ****Yes**** → Do not prescribe ArmaForce. Consider a suitable alternative.
- ****No**** → Proceed to step 4.

4. Assess Prior Use of ArmaForce

- Has the patient used ArmaForce before without experiencing adverse effects?
- ****Yes**** → Inform of potential anaphylaxis associated with Andrographis and Echinacea use. Educate on symptoms and immediate action. Proceed to step 5.
- ****No**** → Proceed to step 5.

5. Educate on Symptoms and Immediate Action

- Educate the patient on recognizing symptoms of anaphylaxis and the importance of stop use and seek immediate medical attention if symptoms occur:
 - Difficult or noisy breathing
 - Swelling of the tongue
 - Swelling or tightness in the throat
 - Wheeze or persistent cough
 - Difficulty talking or a hoarse voice

- Persistent dizziness or collapse

6. Finalise Prescribing Decision

- If the patient is aware of label warnings, and no contraindications are identified, you may consider prescribing ArmaForce per the label instructions “Adults: Take 1 tablet once a day for a maximum of two weeks.”

FINAL OVERSTICKER (ONE SIZE FOR ALL SKUS)

Document 4



BioCeuticals



9 337896 003459

EXP:

DIRECTIONS FOR USE: Adults: Take 1 tablet once a day for a maximum of two weeks.

INDICATIONS: ArmaForce® is a comprehensive formula combining scientifically tested andrographis, standardised herbs and immune-supporting nutrients. Andrographis decreases the severity of symptoms of mild upper respiratory tract infections, including sore throat, headache, runny nose, cough, fatigue and restless sleep. Zinc and vitamin C maintain healthy immune system function.

WARNINGS: Adults only. Andrographis may cause taste disturbance, including loss of taste, loss of appetite, vomiting and abdominal discomfort. Andrographis may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis) or develop any adverse symptoms, stop use and seek immediate medical attention. Do not use during pregnancy or breastfeeding. Dietary supplements can only be of assistance if dietary intake is inadequate. If symptoms persist, talk to your health professional. Do not use if seal on cap is broken. Store below 30°C.

BioCeuticals® A division of Backmores Ltd, Level 4, 64 Kippax Street, Surry Hills NSW 2010, ph: (+61) 2 9080 0900 www.bioceticals.com.au

ArmaForce®

Relieves Common Cold/Flu and Mild URTI Symptoms

WARNING - Do not use if you have any history of severe allergic reaction. Andrographis may cause anaphylaxis. If swelling of the mouth, throat or difficulty breathing occurs, stop use and seek immediate medical attention.

60

TABLETS

Vegan

AUST L 240712

DIETARY SUPPLEMENT

PRACTITIONER ONLY

ACTIVE INGREDIENTS:

Each tablet contains:

Herbals:

Andrographis paniculata (andrographis) extract dry conc. AP Bio®	178.6 mg
equiv. dry leaf 2.5 g, std. to contain: andrographolides 62.5 mg	
Olea europaea (olive) extract dry conc.	150 mg
equiv. dry leaf 750 mg, std. to contain: oleuropein 30 mg	
Echinacea purpurea (echinacea) extract dry conc.	125 mg
equiv. dry root 750 mg, std. to contain: chlorogenic acid 250 micrograms	
Nutrients:	
Ascorbic acid (vitamin C)	250 mg
Zinc amino acid chelate (zinc 5 mg)	25 mg

Made in Australia.

AP-Bio® is a trademark of Natural Remedies Pvt. Ltd.




WARNING - Do not use if you have any history of severe allergic reaction. Andrographis may cause anaphylaxis. If swelling of the mouth, throat or difficulty breathing occurs, stop use and seek immediate medical attention.

s47G

FINAL LABEL (60s)


BioCeuticals

9 537866 003459



EXP.

DIRECTIONS FOR USE: Adults: Take 1 tablet once a day for a maximum of two weeks.

INDICATIONS: ArmaForce® is a comprehensive formula combining scientifically tested andrographis, standardised herbs and immune-supporting nutrients. Andrographis decreases the severity of symptoms of mild upper respiratory tract infections, including sore throat, headache, runny nose, cough, fatigue and restless sleep. Zinc and vitamin C maintain healthy immune system function.

WARNINGS: Adults only. Andrographis may cause taste disturbance, including loss of taste, loss of appetite, vomiting and abdominal discomfort. Andrographis may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis) or develop any adverse symptoms, stop use and seek immediate medical attention. Do not use during pregnancy or breastfeeding. Dietary supplements can only be of assistance if dietary intake is inadequate. If symptoms persist, talk to your health professional. Do not use if seal on cap is broken. Store below 30°C.

BioCeuticals® A division of Blackmores Ltd, Level 4, 64 Kippax Street, Sunny Hills NSW 2010, ph: (+61) 2 9080 0900 www.bioceuticals.com.au

ArmaForce®

Relieves Common Cold/Flu and Mild URTI Symptoms

WARNING - Do not use if you have any history of severe allergic reaction. Andrographis may cause anaphylaxis. If swelling of the mouth, throat or difficulty breathing occurs, stop use and seek immediate medical attention.

60 TABLETS

Vegan
AUST L 340712
DIETARY SUPPLEMENT
PRACTITIONER ONLY

ACTIVE INGREDIENTS:
Each tablet contains:

Herbals:

Andrographis paniculata (andrographis) extract dry conc. AP Bio®	178.6 mg
equiv. dry leaf 2.5 g, std. to contain:	
andrographolides 62.5 mg	
Olea europaea (olive) extract dry conc.	150 mg
equiv. dry leaf 750 mg, std. to contain:	
oleuropein 30 mg	
Echinacea purpurea (echinacea) extract dry conc.	125 mg
equiv. dry root 750 mg, std. to contain	
cichoric acid 250 micrograms	

Nutrients:

Ascorbic acid (vitamin C)	250 mg
Zinc amino acid chelate (zinc 5 mg)	25 mg

Made in Australia.

AP-Bio® is a trademark of Natural Remedies Pvt. Ltd.




From: [s.22](#)
To: [ADR Reports](#)
Cc: [Product Safety](#)
Subject: RE: INFORM: Urgent Implementation of Safety Measures for ArmaForce - Mitigating Anaphylaxis Risk [SEC=OFFICIAL]
Date: Wednesday, 3 July 2024 7:12:28 PM
Attachments: [image002.png](#)
[image008.png](#)
[image009.png](#)
[image010.png](#)
[Attachment 1. DRAFT Dear HCP letter Armaforce 030724.docx](#)
[Attachment 2. DRAFT New Armaforce Prescribing Decision Tree 030724.docx](#)
[Attachment 3. DRAFT WARNING BC ArmaForce \(60\) LAB V4 3.pdf](#)

Dear 

Thank you for your communication regarding the updates and proposals for ArmaForce [s.22](#) .

[s47G](#) 

Please find below our responses to your comments:

1. **Dear HCP Letter:** We appreciate the TGA's feedback and have incorporated the suggested updates in Attachment 1.
2. **Prescribing Tree Update:** In response to the TGA's remarks, we have revised the Prescribing Tree. The amendments can be found in Attachment 2.
3. **New Label Warning Box for ArmaForce:** We acknowledge the challenge posed by the repetition of warnings on smaller pack sizes. To resolve this, we have amalgamated the existing TGA mandatory label warning for allergic reaction with the new contraindication warning box, ensuring the message remains consistent with the version previously approved by the TGA. The revised new label warning box in Attachment 3. To further enhance visibility, we have employed a bold typeface for the new label warning box, with the position aligning with other known box warnings.

[s.22](#) 

s.22

We trust this addresses TGA's queries and look forward to TGA's confirmation to proceed with the proposed updates. Should you require any further information or clarification, please do not hesitate to contact me.

Regards,



From: ADR Reports <ADR.Reports@health.gov.au>

Sent: Tuesday, July 2, 2024 1:51 PM

To: [REDACTED]@blackmores.com.au; ADR Reports <ADR.Reports@health.gov.au>

Cc: Product Safety <productsafety@blackmores.com.au>

Subject: RE: INFORM: Urgent Implementation of Safety Measures for ArmaForce - Mitigating Anaphylaxis Risk [SEC=OFFICIAL]

Caution - External Sender

This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear [REDACTED]

Thank you for your updated proposals. Can you please advise if you have also put stock of [REDACTED] on hold, as discussed in s.22 [REDACTED] email below?

We have some further comments on your proposals as follow:

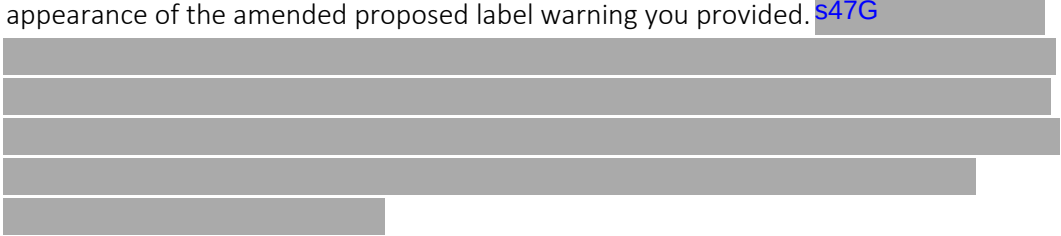
1. Dear HCP Letter:

New Contraindication: '.....ArmaForce is contraindicated for use in individuals with any history of severe allergic reaction (anaphylaxis) to any substance.' To align with point 1 and proposed label warning, severe allergic reaction and anaphylaxis should be listed separately as the proposed wording implies the contraindication is only for anaphylaxis.

Prescribing Instructions: The instructions should be expanded to be clear that these are for both new and previous users of ArmaForce.

Pose these questions to all patient: Patients should be clearly informed that anaphylaxis can develop even after prior use without any reactions – the proposed wording instructs to ask patients but does not advise to inform. Patients should also be advised that if they have experienced mild reactions in the past, to ArmaForce, Andrographis, or Echinacea they should not use ArmaForce, as sometimes a mild

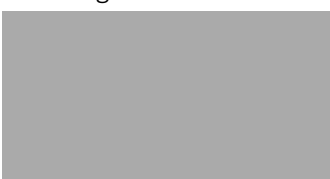
reaction occurs before a more severe reaction, including anaphylaxis (please see [TGA Andrographis paniculata safety advisory](#) – you may wish to also include a link to this in the dear HCP letter).

2. **Prescribing Tree Update:** under point 4, patients should be clearly informed that anaphylaxis can develop even after prior use without any reactions.
3. **New Label Warning Box for ArmaForce:** The TGA does not object to the wording and appearance of the amended proposed label warning you provided. [s47G](#)

4. [s47G](#) 
[s.22](#) ? 
5. **Website and Brand Updates:** Please advise when this will be launched, and whether this also applies to [s47G](#) and [s.22](#)

6. [s.22](#) 

Please let me know if you have any questions, otherwise please provide a response to the above questions by **5pm Thursday 4 June 2024**.

Kind regards



Adverse Event and Medicine Defect Section
Pharmacovigilance Branch

Phone: 02 6289 2709

Email: adr.reports@health.gov.au

Therapeutic Goods Administration
Australian Government, Department of Health and Aged Care
PO Box 100
Woden ACT 2606
www.tga.gov.au



Important: This transmission is intended only for the use of the addressee and may contain confidential or legally privileged information. If you are not the intended recipient, you are notified that

Subject: Important Safety Information Regarding ArmaForce - Risk of Anaphylaxis

Dear Healthcare Professional (HCP),

Safety Statement: Please be advised that this letter contains critical safety information about the prescription of ArmaForce, particularly concerning the risk of anaphylaxis associated with Andrographis. It is imperative to adhere to the updated prescribing guidelines to ensure patient safety. Please see <https://www.tga.gov.au/news/safety-alerts/medicines-containing-andrographis-paniculata-safety-advisory>

New Contraindication: Effective immediately, ArmaForce is contraindicated for use in individuals with any history of severe allergic reaction. This precaution is based on recent adverse event reports and aims to ensure patient safety.

Prescribing Instructions: When considering ArmaForce for your patients, please consider the below for both new and previous users of Armaforce:

1. **Inquire about any history of allergic reactions or anaphylaxis** to any substance, regardless of its relation to the ingredients in ArmaForce. Advise patients against using ArmaForce if they have ever experienced a severe allergic reaction or anaphylactic reaction to any substance.
2. **Specifically ask about previous reactions** to ArmaForce or its active ingredients, Andrographis and Echinacea species (Echinacea). If patients have had any type of allergic reactions after taking medicines containing these ingredients, they should not use ArmaForce.
3. **Inform all patients**, even if they have used ArmaForce previously without adverse effects, that anaphylaxis can develop even after prior use without any reactions. If patients had experienced an allergic reaction to a medicine containing both andrographis and echinacea, they should avoid using Armaforce.
4. **Emphasize the urgency of seeking immediate medical attention** if patients experience any signs of a reaction. The following symptoms warrant prompt medical intervention:
 - Difficult or noisy breathing
 - Swelling of the tongue
 - Swelling or tightness in the throat
 - Wheeze or persistent cough
 - Difficulty talking or a hoarse voice
 - Persistent dizziness or collapse

Patient Education: Please ensure that patients are fully informed about the contraindications associated with ArmaForce and understand the importance of immediate medical attention if symptoms of anaphylaxis occur.

Product Supply: The product label will be updated with the new contraindication. This will be applied across ArmaForce 30s (), 60s () and 120s (). This means that these products will be temporarily OOS until approximately mid-August.

Thank you for your attention to this important safety information. Your cooperation is essential in maintaining the well-being of your patients.

Sincerely,

[Name]

[Title]

[Contact Information]

ArmaForce® Prescribing Decision Tree with updated label warning.**WARNINGS:**

Allergic Reactions: Some individuals may experience allergic reactions to Andrographis. In the event of a severe reaction such as anaphylaxis, or if any adverse symptoms develop, discontinue use immediately and seek medical attention.

Severe Allergic Reaction History: Do not use ArmaForce if you have a history of severe allergic reactions. Andrographis may cause anaphylaxis. If symptoms such as swelling of the mouth or throat, or difficulty breathing occur, stop use and seek immediate medical attention.

Taste Disturbance: Andrographis may cause taste disturbances, including loss of taste, loss of appetite.

Gastrointestinal: Andrographis may cause vomiting and abdominal discomfort.

Adults Only: ArmaForce is intended for use by adults only.

Pregnancy/Breastfeeding Contraindication: Do not use ArmaForce if pregnant or breastfeeding.

1. Patient Eligibility

- Is the patient an adult and not pregnant or breastfeeding?
- ****No**** → Do not prescribe ArmaForce. Consider a suitable alternative.
- ****Yes**** → Proceed to step 2.

2. Allergy and Anaphylaxis History

- Has the patient ever had a severe allergic reaction or anaphylaxis?
- ****Yes**** → Do not prescribe ArmaForce. Consider a suitable alternative.
- ****No**** → Proceed to step 3.

3. Previous Reactions to Andrographis or Echinacea

- Has the patient previously reacted to Andrographis or Echinacea?
- ****Yes**** → Do not prescribe ArmaForce. Consider a suitable alternative.
- ****No**** → Proceed to step 4.

4. Assess Prior Use of ArmaForce

- Has the patient used ArmaForce before without experiencing adverse effects?
- ****Yes**** → Inform of potential anaphylaxis associated with Andrographis and Echinacea use. Educate on symptoms and immediate action. Proceed to step 5.
- ****No**** → Inform patient that anaphylaxis can develop even after prior use without any reactions. Proceed to step 5.

5. Educate on Symptoms and Immediate Action

- Educate the patient on recognizing symptoms of anaphylaxis and the importance of stop use and seek immediate medical attention if symptoms occur:
 - Difficult or noisy breathing
 - Swelling of the tongue
 - Swelling or tightness in the throat
 - Wheeze or persistent cough

- Difficulty talking or a hoarse voice
- Persistent dizziness or collapse

6. Finalise Prescribing Decision

- If the patient is aware of label warnings, and no contraindications are identified, you may consider prescribing ArmaForce per the label instructions "Adults: Take 1 tablet once a day for a maximum of two weeks."

s47G



From: S.22
To: ADR Reports
Cc: Product Safety; [REDACTED]
Subject: RE: INFORM: Urgent Implementation of Safety Measures for ArmaForce - Mitigating Anaphylaxis Risk [SEC=OFFICIAL]
Date: Tuesday, 9 July 2024 8:28:50 PM
Attachments: [image001.png](#)
[image003.png](#)
[image004.png](#)
[image005.png](#)
[Attachment 1. Dear HCP letter Armaforce FINAL.docx](#)
[Attachment 2. New Armaforce Prescribing Decision Tree FINAL.docx](#)
[Attachment 3. WARNING FINAL BC ArmaForce \(60\) LAB V3.pdf](#)

Dear S.22,

Thank you for the meeting with [REDACTED] and [REDACTED] this afternoon.

We confirm that we have implemented the changes requested by the Therapeutic Goods Administration (TGA) to the Dear Healthcare Professional (HCP) letter.

We would like to express our appreciation for the TGA's constructive discussions, thorough review, and valuable input regarding the label box warning, the Dear HCP letter, the Armaforce prescribing decision tree, and the application of the ancillary label. We are committed to enhancing the safety information provided to healthcare professionals and patients alike.

Furthermore, we confirm that Blackmores is fully committed to the immediate implementation of the safety measures discussed. Our team is diligently working on the labels tonight to ensure prompt implementation.

For your reference, please find attached:

1. The revised Dear HCP letter (Attachment 1)
2. The Armaforce Prescribing Decision Tree (Attachment 2)
3. The new label, and oversticker/ancillary label for Armaforce (Attachment 3)

Thank you once again for your support and partnership in ensuring patient safety.

Regards,

S.22

BLACKMORES®
| GROUP

From: ADR Reports <ADR.Reports@health.gov.au>

Sent: Tuesday, July 9, 2024 6:30 PM

To: S.22 @blackmores.com.au; Product Safety

<productsafety@blackmores.com.au>

Subject: RE: INFORM: Urgent Implementation of Safety Measures for ArmaForce - Mitigating Anaphylaxis Risk [SEC=OFFICIAL]

Caution - External Sender

This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear s.22 ,

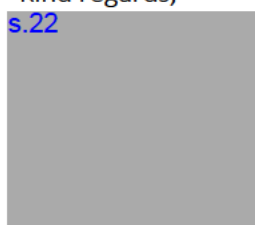
Thank you for the video meeting this afternoon.

As briefly discussed today and in our phone call last Friday, we consider the wording in the Dear HCP letter should make it clearer in Points 2 and 3 that patients should be asked about any reactions to ArmaForce or its active ingredients, Andrographis **or** Echinacea, and should make it clear that if patients have had any type of allergic reactions after taking medicines containing either of these ingredients, they should not use ArmaForce. This should also be reflected in Point 3, where patients should be advised to avoid using ArmaForce if they had experienced an allergic reaction to a medicine containing either Andrographis or Echinacea. As written, it could be taken to mean medicines containing both Andrographis and Echinacea, however at this stage it is not known whether sensitisation is occurring to both ingredients together or to only one, therefore a cautious approach is appropriate.

We await your email confirmation of your commitment to the 2nd proposed version of the label warning and ancillary label.

Kind regards,

s.22



Adverse Event & Medicine Defect Section
Pharmacovigilance Branch

s.22



Therapeutic Goods Administration
Australian Government, Department of Health and Aged Care
PO Box 100
Woden ACT 2606
www.tga.gov.au



Subject: Important Safety Information Regarding ArmaForce - Risk of Anaphylaxis

Dear Healthcare Professional (HCP),

Safety Statement: Please be advised that this letter contains critical safety information about the prescription of ArmaForce, particularly concerning the risk of anaphylaxis associated with Andrographis. It is imperative to adhere to the updated prescribing guidelines to ensure patient safety. Please see <https://www.tga.gov.au/news/safety-alerts/medicines-containing-andrographis-paniculata-safety-advisory>

New Contraindication: Effective immediately, ArmaForce is contraindicated for use in individuals with any history of severe allergic reaction. This precaution is based on recent adverse event reports and aims to ensure patient safety.

Prescribing Instructions: When considering ArmaForce for your patients, please consider the below for both new and previous users of Armaforce:

1. **Inquire about any history of allergic reactions or anaphylaxis** to any substance, regardless of its relation to the ingredients in ArmaForce. Advise patients against using ArmaForce if they have ever experienced a severe allergic reaction or anaphylactic reaction to any substance.
2. **Specifically ask about previous reactions** to ArmaForce or its active ingredients, Andrographis or Echinacea species (Echinacea). If patients have had any type of allergic reactions after taking medicines containing either of these ingredients, they should not use ArmaForce.
3. **Inform all patients**, even if they have used ArmaForce previously without adverse effects, that anaphylaxis can develop even after prior use without any reactions. If patients had experienced an allergic reaction to a medicine containing either andrographis or echinacea, they should avoid using Armaforce.
4. **Emphasize the urgency of seeking immediate medical attention** if patients experience any signs of a reaction. The following symptoms warrant prompt medical intervention:
 - Difficult or noisy breathing
 - Swelling of the tongue
 - Swelling or tightness in the throat
 - Wheeze or persistent cough
 - Difficulty talking or a hoarse voice
 - Persistent dizziness or collapse

Patient Education: Please ensure that patients are fully informed about the contraindications associated with ArmaForce and understand the importance of immediate medical attention if symptoms of anaphylaxis occur.

Product Supply: The product label will be updated with the new contraindication. This will be applied across ArmaForce 30s (s47G), 60s (s47G) and 120s (s47G). This means that these products will be temporarily OOS until approximately mid-August.

Thank you for your attention to this important safety information. Your cooperation is essential in maintaining the well-being of your patients.

Sincerely,

[Name]

[Title]

[Contact Information]

ArmaForce® Prescribing Decision Tree with updated label warning.**WARNINGS:**

Allergic Reactions: Some individuals may experience allergic reactions to Andrographis. In the event of a severe reaction such as anaphylaxis, or if any adverse symptoms develop, discontinue use immediately and seek medical attention.

Severe Allergic Reaction History: Do not use ArmaForce if you have a history of severe allergic reactions. Andrographis may cause anaphylaxis. If symptoms such as swelling of the mouth or throat, or difficulty breathing occur, stop use and seek immediate medical attention.

Taste Disturbance: Andrographis may cause taste disturbances, including loss of taste, loss of appetite.

Gastrointestinal: Andrographis may cause vomiting and abdominal discomfort.

Adults Only: ArmaForce is intended for use by adults only.

Pregnancy/Breastfeeding Contraindication: Do not use ArmaForce if pregnant or breastfeeding.

1. Patient Eligibility

- Is the patient an adult and not pregnant or breastfeeding?
- ****No**** → Do not prescribe ArmaForce. Consider a suitable alternative.
- ****Yes**** → Proceed to step 2.

2. Allergy and Anaphylaxis History

- Has the patient ever had a severe allergic reaction or anaphylaxis?
- ****Yes**** → Do not prescribe ArmaForce. Consider a suitable alternative.
- ****No**** → Proceed to step 3.

3. Previous Reactions to Andrographis or Echinacea

- Has the patient previously reacted to Andrographis or Echinacea?
- ****Yes**** → Do not prescribe ArmaForce. Consider a suitable alternative.
- ****No**** → Proceed to step 4.

4. Assess Prior Use of ArmaForce

- Has the patient used ArmaForce before without experiencing adverse effects?
- ****Yes**** → Inform of potential anaphylaxis associated with Andrographis and Echinacea use. Educate on symptoms and immediate action. Proceed to step 5.
- ****No**** → Inform patient that anaphylaxis can develop even after prior use without any reactions. Proceed to step 5.

5. Educate on Symptoms and Immediate Action

- Educate the patient on recognizing symptoms of anaphylaxis and the importance of stop use and seek immediate medical attention if symptoms occur:
 - Difficult or noisy breathing
 - Swelling of the tongue
 - Swelling or tightness in the throat
 - Wheeze or persistent cough

- Difficulty talking or a hoarse voice
- Persistent dizziness or collapse

6. Finalise Prescribing Decision

- If the patient is aware of label warnings, and no contraindications are identified, you may consider prescribing ArmaForce per the label instructions “Adults: Take 1 tablet once a day for a maximum of two weeks.”

FINAL OVERSTICKER (ONE SIZE FOR ALL SKUS)

Document 6


BioCeuticals



9 337896 003459

EXP:

DIRECTIONS FOR USE: Adults: Take 1 tablet once a day for a maximum of two weeks.

INDICATIONS: ArmaForce® is a comprehensive formula combining scientifically tested andrographis, standardised herbs and immune-supporting nutrients. Andrographis decreases the severity of symptoms of mild upper respiratory tract infections, including sore throat, headache, runny nose, cough, fatigue and restless sleep. Zinc and vitamin C maintain healthy immune system function.

WARNINGS: Adults only. Andrographis may cause taste disturbance, including loss of taste, loss of appetite, vomiting and abdominal discomfort. Andrographis may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis) or develop any adverse symptoms, stop use and seek immediate medical attention. Do not use during pregnancy or breastfeeding. Dietary supplements can only be of assistance if dietary intake is inadequate. If symptoms persist, talk to your health professional. Do not use if seal on cap is broken. Store below 30°C.

BioCeuticals® A division of Backmores Ltd, Level 4, 64 Kippax Street, Surry Hills NSW 2010, ph: (+61) 2 9080 0900 www.biocellulars.com.au

ArmaForce®

Relieves Common Cold/Flu and Mild URTI Symptoms

WARNING - Do not use if you have any history of severe allergic reaction. Andrographis may cause anaphylaxis. If swelling of the mouth, throat or difficulty breathing occurs, stop use and seek immediate medical attention.

60

TABLETS

Vegan

AUST L 240712

DIETARY SUPPLEMENT

PRACTITIONER ONLY

ACTIVE INGREDIENTS:

Each tablet contains:

Herbals:

Andrographis paniculata (andrographis) extract dry conc. AP Bio®	178.6 mg
equiv. dry leaf 2.5 g, std. to contain: andrographolides 62.5 mg	
Olea europaea (olive) extract dry conc.	150 mg
equiv. dry leaf 750 mg, std. to contain: oleuropein 30 mg	
Echinacea purpurea (echinacea) extract dry conc.	125 mg
equiv. dry root 750 mg, std. to contain: chlorogenic acid 250 micrograms	
Nutrients:	
Ascorbic acid (vitamin C)	250 mg
Zinc amino acid chelate (zinc 5 mg)	25 mg

Made in Australia.

AP-Bio® is a trademark of Natural Remedies Pvt. Ltd.




WARNING - Do not use if you have any history of severe allergic reaction. Andrographis may cause anaphylaxis. If swelling of the mouth, throat or difficulty breathing occurs, stop use and seek immediate medical attention.

s47G

FINAL LABEL (60s)


BioCeuticals



9 537866 003459 >

Ⓢ
EXP.

DIRECTIONS FOR USE: Adults: Take 1 tablet once a day for a maximum of two weeks.

INDICATIONS: ArmaForce® is a comprehensive formula combining scientifically tested andrographis, standardised herbs and immune-supporting nutrients. Andrographis decreases the severity of symptoms of mild upper respiratory tract infections, including sore throat, headache, runny nose, cough, fatigue and restless sleep. Zinc and vitamin C maintain healthy immune system function.

WARNINGS: Adults only. Andrographis may cause taste disturbance, including loss of taste, loss of appetite, vomiting and abdominal discomfort. Andrographis may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis) or develop any adverse symptoms, stop use and seek immediate medical attention. Do not use during pregnancy or breastfeeding. Dietary supplements can only be of assistance if dietary intake is inadequate. If symptoms persist, talk to your health professional. Do not use if seal on cap is broken. Store below 30°C.

BioCeuticals® A division of Blackmores Ltd, Level 4, 64 Kippax Street, Sunny Hills NSW 2010, ph: (+61) 2 9080 0900 www.bioceuticals.com.au

ArmaForce®

Relieves Common Cold/Flu and Mild URTI Symptoms

WARNING - Do not use if you have any history of severe allergic reaction. Andrographis may cause anaphylaxis. If swelling of the mouth, throat or difficulty breathing occurs, stop use and seek immediate medical attention.

60

TABLETS

ACTIVE INGREDIENTS:
Each tablet contains:

Herbals:

Andrographis paniculata (andrographis) extract dry conc. AP Bio®	178.6 mg
equiv. dry leaf 2.5 g, std. to contain: andrographolides 62.5 mg	
Olea europaea (olive) extract dry conc. equiv. dry leaf 750 mg, std. to contain: oleuropein 30 mg	150 mg
Echinacea purpurea (echinacea) extract dry conc. equiv. dry root 750 mg, std. to contain: cichoric acid 250 micrograms	125 mg

Nutrients:

Ascorbic acid (vitamin C)	250 mg
Zinc amino acid chelate (zinc 5 mg)	25 mg

Made in Australia.

AP-Bio® is a trademark of Natural Remedies Pvt. Ltd.

AP-Bio 



From: [ADR Reports](#)
To: [S.22](#)
Cc: [Product Safety](#); [REDACTED]
Subject: RE: INFORM: Urgent Implementation of Safety Measures for ArmaForce - Mitigating Anaphylaxis Risk [SEC=OFFICIAL]
Date: Wednesday, 10 July 2024 10:58:38 AM
Attachments: [image001.png](#)
[image003.png](#)
[image004.png](#)
[image005.png](#)

Dear [S.22](#)

Thank you for your email. As discussed in the meeting we have no objections to your latest proposals as an interim measure. However as also mentioned in the meeting and in a previous email, we are actively considering the suitability of the ingredient *Andrographis paniculata* in listed medicines. The outcome of our review may result in a different regulatory action and we cannot confirm that your proposed interim measures are appropriate to mitigate the risks, particularly in the longer term. Any changes to regulatory requirements will be communicated following our usual processes.

We are also actively monitoring adverse events, and cannot exclude the need for additional more immediate action.

Thank you again for your co-operation.

Kind regards,

[S.22](#)

Adverse Event & Medicine Defect Section
Pharmacovigilance Branch

Email: adr.reports@health.gov.au

Therapeutic Goods Administration
Australian Government, Department of Health and Aged Care
PO Box 100
Woden ACT 2606
www.tga.gov.au

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The Department of Health and Aged Care acknowledges First Nations peoples as the Traditional Owners of Country throughout Australia, and their continuing connection to land, sea and community. We pay our respects to them and



Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration

TGA Reference: [D24-2843013](#)

The Managing Director
FIT-BioCeuticals Pty Ltd
Care of Blackmores Ltd
PO Box 1725
Warriewood NSW 2102

Email: [s.22](#) [@blackmores.com.au; productsafety@blackmores.com.au](#)

Dear Sir/Madam

**Notice under section 31(2) of the
Therapeutic Goods Act 1989
Requirement to provide information or documents**

Re: ArmaForce (AUST L 118578)

ArmaForce (AUST L 297314)

ArmaForce (AUST L 310158)

ArmaForce (AUST L 340712)

ArmaForce Day & Night (AUST L 315991)

ArmaForce Day & Night (AUST L 372558)

[s.22](#)

I refer to ArmaForce (AUST L 118578), ArmaForce (AUST L 297314), ArmaForce (AUST L 310158), ArmaForce (AUST L 340712), ArmaForce Day & Night (AUST L 315991), ArmaForce Day & Night (AUST L 372558) and [s.22](#) (the **medicines**) listed or previously listed on the Australian Register of Therapeutic Goods (**ARTG**) in the name of FIT-BioCeuticals Pty Ltd (**you**).

I am a delegate of the Secretary of the Department of Health and Aged Care for the purposes of paragraph 31 of the *Therapeutic Goods Act 1989* (**the Act**). In accordance with subsection 31(2) of the Act¹, I am writing to require that you provide information as detailed below.

¹ A copy of the Act can be accessed from <http://www.comlaw.gov.au>



Please ensure we receive your response by:

5:00pm 1 August 2024

Please send your response to adr.reports@health.gov.au.

Background

The Therapeutic Goods Administration (TGA) is investigating allergic/hypersensitivity and anaphylactic reactions in association with listed medicines containing the herbal ingredient *Andrographis paniculata* (Andrographis). A [safety review](#) concerning this issue was published in 2015. [Labelling requirements](#) were introduced in 2019 to require all listed medicines containing Andrographis to include the following label warning statement:

'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).

This requirement was implemented as a high-moderate risk change to the Therapeutic Goods (Permissible Ingredients) Determination to warn consumers of the risk of allergic reactions and anaphylaxis in some individuals.

The TGA has continued to monitor reports of allergy and anaphylaxis for medicines containing Andrographis. Since 2005, the TGA has received over 300 reports of anaphylaxis and/or hypersensitivity reactions to medicines containing Andrographis. More than 200 of these reports have been received since 2019. In June 2024, we received a report of an anaphylactic reaction with a fatal outcome in someone that had used a medicine containing Andrographis.

A safety advisory was published on 2 July 2024², warning consumers and healthcare professionals about the potential for severe allergic reactions, including anaphylaxis, in association with medicines containing Andrographis.

To inform our ongoing review of this issue, I am writing to you now, in accordance with section 31 of the Act, to require you to provide the information and documents set out below to assist with our investigation into the medicines.

Required information and documents

Under subsections 31(2) of the Act, as a delegate of the Secretary, I require you to provide the information and documents set out below, and in the form as specified below, that relate to the safety of the medicines.

For each of the medicines, please provide:

- 1) The label for the medicine, including its revision number.

² <https://www.tga.gov.au/news/safety-alerts/medicines-containing-andrographis-paniculata-safety-advisory>

If applicable, you must provide the labels for all packaging types (e.g. blister packs, bottles, sachets, etc.) and pack sizes, including any package inserts or leaflets.



Providing the label

It is preferable that, in place of actual labels, signature-approved scaled copies of labels are provided to us electronically (e.g. PDF), accompanied by a copy of an excerpt from the batch manufacturing record which contains the sample label.

- 2) Details of any serious or non-serious adverse event reports for the medicine, not previously submitted to the TGA, that could be associated with a hypersensitivity reaction or allergic reaction (including anaphylactic reaction). These reactions may be submitted through the online portal, submitted as individual CIOMS forms and/or presented in a spreadsheet and should include, but are not limited to, the following details; medicine name and AUST L (if known), date Adverse Drug Reaction (ADR) received, reaction terms, reaction narrative and patient identifier (e.g. patient initials or age/gender but not full name of patient). If submitted through the online portal please advise of this in your response.

- 3) In addition to the report details in item 2, you are required to provide summary data on the total number of all serious and non-serious hypersensitivity/allergic reaction reports (not including anaphylactic reactions) received for the years 2019, 2020, 2021, 2022, 2023 and 2024 (to 15 June 2024).

These data are to be supplied in the '*Hypersensitivity ADR reports*' of the spreadsheet attached to the email with this s31 Notice.

- 4) In addition to the report details in item 2, you are required to provide the total number of all anaphylactic reaction reports received for the years 2019, 2020, 2021, 2022, 2023 and 2024 (to 15 June 2024).

Please provide these details in the '*Anaphylaxis ADR reports*' tab of the spreadsheet attached to the email with this s31 Notice.

- 5) For each pack size of the medicines, provide details of the number of units (containers/bottles/boxes) you have supplied each year to the Australian market from 1 January 2019 to 31 May 2024.

These data are to be supplied in the '*Supply data*' tab of the spreadsheet attached to the email with this s31 Notice.

- 6) Maximum daily dose of the medicine.

These data are to be supplied these details in the '*Andrographolide & dose*' tab of the spreadsheet attached to the email with this s31 Notice.

- 7) The andrographolide content per dosage unit (mg) if known.

These data are to be supplied in the '*Andrographolide & dose*' tab of the spreadsheet attached to the email with this s31 Notice.

- 8) The name of the Andrographis extract ingredient and the name and address of the manufacturer of the Andrographis extract ingredient.

These data are to be supplied in the '*Andrographolide & dose*' tab of the spreadsheet attached to the email with this s31 Notice.

How to respond to the notice

You are required to provide the above information as soon as possible, but no later than **5 pm, 1 August 2024**. Please contact me immediately if you determine that the timeframe for a response is not practical.

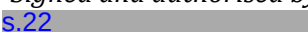
Information and documents should be provided electronically in a readily accessible format. Please contact me immediately if you are unable to supply the required information in this way.

Please note that it is an offence under subsection 31(4) of the Act if you fail to comply with this notice without reasonable excuse. Any failure to reply to this notice by the due date may also result in other regulatory action such as proposal to cancel and/or cancellation of the medicines. If you provide false or misleading material in response to this request you may be subject to criminal penalties under subsection 31(6) of the Act.

We will only be emailing this letter to your company. It is your responsibility to forward this correspondence to any agents or other parties acting on your behalf.

Yours sincerely

Signed and authorised by

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Delegate of the Secretary
Pharmacovigilance Branch

Telephone: 02 5132 0955

Email: adr.reports@health.gov.au

11 July 2024

s.22

Delegate of the Secretary
Pharmacovigilance Branch
Telephone:
Email: adr.reports@health.gov.au
TGA Reference: D24-3189161

27 August 2024

Dear ,

Re: TGA Section 31 notice - BioCeuticals Armaforce (AUST L 310158 and 340712)

Thank you for TGA's notice under section 31(2) of the Therapeutic Goods Act 1989 (**the Act**), dated 5 August 2024, regarding ArmaForce (AUST L 310158 and AUST L 340712) (**Armaforce**). We appreciate the opportunity to provide a benefit-risk analysis that considers the new contraindication label warning of the medicines: "Do not use if you have any history of severe allergic reaction", as required by the notice. In response to TGA's request, please find below BioCeuticals' submission.

Executive summary

This document provides a benefit-risk analysis for BioCeuticals Armaforce in response to the TGA section 31 notice dated 5 August 2024.

The benefit-risk analysis is based on the available data on the safety and efficacy of Armaforce, s47G

. The benefit-risk analysis also considers the safety measures implemented by BioCeuticals to mitigate the risk of anaphylaxis associated with Armaforce, as well as the comparison of the safety measures for similar cases of death due to anaphylaxis in Australia and other countries.

The following are the main findings of the benefit-risk analysis:

Armaforce is a herbal medicine intended to support immune function and relieve cold and flu symptoms. Armaforce contains five ingredients: Andrographis paniculata, Olive leaf extract, Echinacea purpurea, Vitamin C and Zinc.

Andrographis paniculata, also known as king of bitters, is a plant native to India and Southeast Asia. It has been used for centuries in traditional medicine, particularly in Ayurvedic and Traditional Chinese Medicine, for various indications, such as respiratory infections, fever, sore throat, and inflammation. It has also been shown to have immunomodulatory, anti-inflammatory, antiviral, and antioxidant properties in preclinical and clinical studies.

Andrographis paniculata has also been associated with rare but serious cases of anaphylaxis, a potentially life-threatening severe allergic reaction that can cause symptoms

such difficult or noisy breathing, swelling of tongue, swelling or tightness in throat, wheeze or persistent cough, difficulty talking or hoarse voice, persistent dizziness or collapse. Anaphylaxis can occur within minutes or hours after exposure to an allergen and requires immediate medical attention and treatment with adrenaline.

The exact mechanism of anaphylaxis caused by *Andrographis paniculata* is not fully elucidated, but it may involve IgE-mediated hypersensitivity, cross-reactivity with other allergens, or non-IgE-mediated mast cell activation. The risk factors for anaphylaxis may include genetic predisposition, previous exposure to *Andrographis paniculata* or related plants, concurrent use of other medications or supplements, and underlying medical conditions such as atopy.

Following the fatal case of anaphylaxis reported in June 2024, BioCeuticals further strengthened the safety measures for Armaforce by adding a new front-of-pack boxed label warning with the contraindication “do not use if you have any history of severe allergic reaction.” This contraindication is intended to prevent the use of Armaforce in patients who are at high risk of anaphylaxis due to previous exposure or sensitivity to *Andrographis* or any ingredients.

BioCeuticals also added an additional warning statement to the front-of-pack boxed warning: “*Andrographis* may cause anaphylaxis. Stop use and seek immediate medical attention if you experience swelling of the mouth, throat or difficulty breathing.” This helps patients to recognise the symptoms that require urgent medical attention.

Additional safety measures to enhance the awareness and education of healthcare professionals and consumers about the risk of anaphylaxis associated with Armaforce was immediately implemented. These measures included electronic direct mails, dear healthcare professional letter, prescribing decision trees, product website updates, box warning additions, over-sticker warnings on warehouse stock, sales representatives’ activation, and pharmacovigilance monitoring and reporting.

BioCeuticals believes that this is an appropriate and proportionate safety measure that is consistent with the current scientific knowledge and the precautionary principle.

The benefit-risk balance of Armaforce remains positive for its intended use and target population, provided that the contraindication and the warning statements are followed.

Armaforce has demonstrated efficacy in supporting immune function and reducing the severity and duration of common cold symptoms in clinical trials and real-world evidence. Armaforce is generally well tolerated. The risk of anaphylaxis associated with Armaforce is rare and can be mitigated by the implementation of the safety measures described above. The benefits of Armaforce outweigh the risks for most patients who do not have a history of severe allergic reaction.

The safety measures implemented by BioCeuticals for Armaforce are comparable to or more stringent than the safety measures for similar cases of death due to anaphylaxis in Australia and other countries. For example, royal jelly, a bee product that has been associated with several cases of fatal anaphylaxis in Australia, is required to carry the following warning statement on the product label:

- “Not suitable for children”
- “Not to be taken by asthma and allergy sufferers” in 3mm type, prominent on front and

- “This product contains royal jelly which has been reported to cause severe allergic reactions and in rare cases fatalities, especially in asthma and allergy sufferers.”

However, there is no contraindication for royal jelly products for patients with a history of severe allergic reaction. The label warning was not implemented as a front-of-pack boxed warning, with lesser prominence compared to the warning on Armaforce.

Similarly, peanut, a common food allergen that has caused many cases of fatal anaphylaxis worldwide, is required to be declared on the food label, but there is no contraindication for peanut products for patients with a history of severe allergic reaction.

Therefore, the new contraindication label warning for Armaforce is consistent with the best practice of risk management and consumer protection.

1. Introduction

This document provides a benefit-risk analysis for BioCeuticals Armaforce that considers the new contraindication label warning of the medicines: “Do not use if you have any history of severe allergic reaction”.

The benefit-risk analysis is based on the available data on the safety and efficacy of Armaforce, ^{s47G} The benefit-risk analysis also considers the safety measures implemented by BioCeuticals to mitigate the risk of anaphylaxis associated with Armaforce, as well as the comparison of the safety measures for similar cases of death due to anaphylaxis in Australia and other countries.

The benefit-risk analysis follows the structure and format of the TGA guideline on benefit-risk assessment of medicines (Version 1.0, July 2020) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guideline on pharmacovigilance planning (E2E). The benefit-risk analysis also uses relevant references from the scientific literature, regulatory documents, and international best practices.

2. Description of Armaforce

2.1 Indication

Armaforce is a herbal medicine indicated to support immune function and relieve cold and flu symptoms.

2.2 Composition

Armaforce contains five ingredients: Andrographis paniculata, Echinacea purpurea, Olive leaf extract, Vitamin C and Zinc. Each tablet of Armaforce contains the following amounts of the active ingredients:

Active ingredient	Amount per tablet
Andrographis paniculata (Andrographis)	178.6mg
equiv. to andrographolides	62.5 mg
Olea europaea (Olive) extract	150 mg
Echinacea purpurea (Echinacea)	125 mg
Ascorbic acid (vitamin C)	250 mg
Zinc amino acid chelate (zinc 5mg)	25 mg

2.3 Dosage

The recommended dosage of Armaforce for adults is as follows:

- Take 1 tablet once a day for a maximum of two weeks.

2.4 Pharmacology

Armaforce contains ingredients that have pharmacological effects on the immune system and the respiratory tract. The main pharmacological effects of each ingredient are summarised below.

2.4.1 *Andrographis paniculata*

Andrographis paniculata, also known as king of bitters, is a plant native to India and Southeast Asia. It has been used in traditional medicine for centuries in various indications, such as respiratory infections, fever, sore throat, and inflammation. It has also been shown to have immunomodulatory, anti-inflammatory, antiviral, and antioxidant properties in preclinical and clinical studies.

The main active constituent of *Andrographis paniculata* is andrographolide, a diterpenoid lactone that can modulate various immune cells and cytokines. Andrographolide can enhance the phagocytic activity of macrophages, the proliferation and activation of T cells and natural killer cells, and the production of antibodies by B cells. Andrographolide can also inhibit the expression of pro-inflammatory cytokines such as interleukin-1 beta (IL-1 β), interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF- α), and interferon-gamma (IFN- γ), and increase the expression of anti-inflammatory cytokines such as interleukin-10 (IL-10) and transforming growth factor-beta (TGF- β). Andrographolide can also suppress the activation of nuclear factor-kappa B (NF- κ B), a key transcription factor involved in inflammation and immunity.

2.4.2 *Echinacea purpurea*

Echinacea purpurea, also known as purple coneflower, is a plant native to North America. It has been used in traditional medicine for wound healing, infections, and inflammation. It has also been shown to have immunostimulatory, anti-inflammatory, antiviral, and antioxidant properties in preclinical and clinical studies.

The main active constituents of *Echinacea purpurea* are polysaccharides, alkylamides, caffeic acid derivatives, and glycoproteins. These compounds can modulate various immune cells and cytokines. Polysaccharides can activate macrophages, natural killer cells, and dendritic cells, and stimulate the production of pro-inflammatory cytokines such as IL-1 β , IL-6, TNF- α , and IFN- γ . Alkylamides can bind to cannabinoid receptors and modulate the immune response by inhibiting the activation of NF- κ B and the expression of pro-inflammatory cytokines. Caffeic acid derivatives can inhibit the activity of hyaluronidase, an enzyme that degrades the extracellular matrix and facilitates the spread of pathogens. Glycoproteins can induce the production of type I interferons and other antiviral cytokines by activating toll-like receptors.

2.4.3 *Olive leaf extract*

Olive leaf extract is derived from the leaves of *Olea europaea*, also known as olive tree, which is native to the Mediterranean region. It has been used in traditional medicine for cardiovascular diseases, diabetes, and infections. It has also been shown to have immunomodulatory, anti-inflammatory, antiviral, and antioxidant properties in preclinical and clinical studies.

The main active constituent of olive leaf extract is oleuropein, a phenolic compound that can modulate various immune cells and cytokines. Oleuropein can activate macrophages, natural killer cells, and T cells, and stimulate the production of pro-inflammatory cytokines such as IL-1 β , IL-6, TNF- α , and IFN- γ . Oleuropein can also inhibit the expression of anti-inflammatory

cytokines such as IL-10 and TGF- β , and modulate the balance between Th1 and Th2 immune responses.

2.4.4 Vitamin C

Ascorbic acid, also known as vitamin C, is a water-soluble vitamin that acts as a cofactor for various enzymes and a potent antioxidant in the body. Ascorbic acid is essential for the synthesis of collagen, carnitine, and catecholamines, and the metabolism of tyrosine, folic acid, and iron. Ascorbic acid is also involved in the regulation of the immune system and the response to infections. Ascorbic acid deficiency can cause scurvy, a disease characterized by bleeding gums, skin lesions, and impaired wound healing.

Ascorbic acid can modulate various immune cells and cytokines. Ascorbic acid can enhance the proliferation and activation of T cells, B cells, natural killer cells, and macrophages, and stimulate the production of pro-inflammatory cytokines such as IL-1 β , IL-6, TNF- α , and IFN- γ . Ascorbic acid can also inhibit the expression of anti-inflammatory cytokines such as IL-10 and TGF- β and modulate the balance between Th1 and Th2 immune responses.

2.4.5 Zinc

Zinc is an essential trace element that plays a vital role in various biological processes, such as cell growth, differentiation, and metabolism. Zinc is also involved in the regulation of the immune system and the response to infections. Zinc deficiency can impair the function and development of various immune cells, such as T cells, B cells, natural killer cells, and macrophages, and increase the susceptibility to infections.

Zinc can modulate various immune cells and cytokines. Zinc can enhance the proliferation and activation of T cells and natural killer cells, and stimulate the production of pro-inflammatory cytokines such as IL-1 β , IL-6, TNF- α , and IFN- γ . Zinc can also inhibit the expression of anti-inflammatory cytokines such as IL-10 and TGF- β , and modulate the balance between Th1 and Th2 immune responses.

3. Safety of Armaforce

3.1 Risk of anaphylaxis

Anaphylaxis is a severe form of allergic reaction that is potentially life-threatening when not treated immediately. The clinical onset can occur within minutes or hours after exposure to an allergen, and it requires immediate medical attention.

The symptoms of anaphylaxis may include:

- Difficult or noisy breathing
- Swelling of tongue
- Swelling or tightness in throat
- Wheeze or persistent cough
- Difficulty talking or hoarse voice
- Persistent dizziness or collapse

Anaphylaxis can be triggered by various substances, such as foods, drugs, insect stings, latex, pollen, animal dander, mould or chemicals. The risk of anaphylaxis depends on the individual's sensitivity to the allergen, the amount and route of exposure, and the presence of other factors, such as asthma, infections, stress or exercise.

The most common causes of anaphylaxis are foods (such as peanuts, tree nuts, shellfish, eggs, milk, sesame and wheat), insect stings (such as bees, wasps and ants), drugs (such as antibiotics, anaesthetics and non-steroidal anti-inflammatory drugs) and latex. The Australasian Society of Clinical Immunology and Allergy (ASCIA) provides guidelines and resources for the diagnosis, management and prevention of anaphylaxis.

3.2 Anaphylaxis reports related to Armaforce in the PV program

Armaforce is a herbal supplement that contains Echinacea purpurea, Andrographis paniculata, olive leaf extract, zinc and vitamin C. These ingredients are generally considered safe and well-tolerated by most people, but some individuals may have allergic reactions to them. The risk of anaphylaxis from Armaforce is extremely low, but it cannot be completely ruled out.

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This prevalence rate is extremely low and indicates that Armaforce is a safe and well-tolerated product, with a very rare risk of fatal anaphylaxis.

However, it is important to note that s47G

The BioCeuticals PV program acknowledges that these reports are voluntary and have limitations.

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Armaforce should not be used by people who have a known allergy or atopy, as they may be more prone to cross-reactions. Consumers and health

professionals should be aware of the signs and symptoms of anaphylaxis and the need for urgent medical attention in case of a severe allergic reaction.

3.3 Potential pathophysiology of anaphylaxis induced by *Andrographis paniculata*

Andrographis paniculata is a herb that has been used for centuries in traditional medicine for various indications, such as respiratory infections, fever, inflammation, and liver disorders.

The main bioactive constituents of *Andrographis paniculata* are diterpenoid lactones, such as andrographolide, neoandrographolide, and 14-deoxy-11,12-didehydroandrographolide, which have been shown to have anti-inflammatory, immunomodulatory, antiviral, antibacterial, antioxidant, and hepatoprotective effects (Akbar, 2011; Burgos et al., 2009).

The exact mechanisms of action of *Andrographis paniculata* in causing anaphylaxis or severe allergy are not fully understood, but some possible hypotheses are:

- *Andrographis paniculata* may act as a hapten, a small molecule that can bind to a protein and elicit an immune response. Haptens can induce the production of IgE antibodies, which can bind to mast cells and basophils and trigger the release of histamine and other inflammatory mediators, leading to anaphylaxis or severe allergy. *Andrographis paniculata* may have a high affinity for binding to human serum albumin, which is the most abundant protein in blood plasma and a common carrier of haptens (Burgos et al., 2009; Ghosh et al., 2018).
- *Andrographis paniculata* may modulate the Th1/Th2 balance, which is the ratio of two types of helper T cells that regulate the immune response. Th1 cells produce cytokines that promote cell-mediated immunity and inflammation, while Th2 cells produce cytokines that promote humoral immunity and allergy. *Andrographis paniculata* may shift the Th1/Th2 balance towards Th2 dominance, which may enhance the production of IgE antibodies and the sensitivity to allergens, resulting in anaphylaxis or severe allergy. *Andrographis paniculata* may also suppress the regulatory T cells, which are responsible for maintaining immune tolerance and preventing autoimmunity and hypersensitivity (Poolsup et al., 2004; Burgos et al., 2009).
- *Andrographis paniculata* may activate the complement system, which is a part of the innate immune system that consists of a series of proteins that can enhance the inflammatory response and the clearance of pathogens. The complement system can be activated by three pathways: the classical pathway, the lectin pathway, and the alternative pathway. *Andrographis paniculata* may activate the classical pathway by binding to IgG or IgM antibodies that are attached to antigens, or the lectin pathway by binding to mannose-binding lectin that is present on the surface of microbes. The activation of the complement system may lead to the formation of anaphylatoxins, such as C3a and C5a, which can induce mast cell degranulation and the release of histamine and other inflammatory mediators, causing anaphylaxis or severe allergy (Burgos et al., 2009; Ghosh et al., 2018).

These hypotheses are based on the existing literature and the pharmacological properties of *Andrographis paniculata*, but they need to be confirmed by further experimental and clinical studies.

3.4. Potential risk factors and preventive strategies for anaphylaxis associated with *Andrographis paniculata*

The risk factors for anaphylaxis or severe allergy caused by *Andrographis paniculata* are not well established, but some possible factors are:

- A history of atopy or plant allergy, which may indicate a genetic predisposition or a cross-reactivity to *Andrographis paniculata* (Ghosh et al., 2018).
- A high dose or a prolonged use of *Andrographis paniculata*, which may increase the exposure and the sensitization to the product (Burgos et al., 2009).
- A co-administration of other products that contain *Andrographis paniculata* or other allergens, which may enhance the allergic response or the interaction with the product (Burgos et al., 2009).

The preventive measures for anaphylaxis or severe allergy caused by *Andrographis paniculata* can include:

- Avoiding the use of *Andrographis paniculata* or other products that contain *Andrographis paniculata*, especially if there is a history of atopy (Ghosh et al., 2018).
- Consulting a health professional before using *Andrographis paniculata* or other products that contain *Andrographis paniculata* and following the recommended dosage and duration of use (Burgos et al., 2009).
- Monitoring for any signs or symptoms of anaphylaxis or severe allergy after using *Andrographis paniculata* and seek immediate medical attention if they occur (Burgos et al., 2009).
- Carrying an adrenaline auto-injector and an antihistamine and knowing how to use them in case of an emergency (Ghosh et al., 2018).

These preventive measures are based on the general principles of managing anaphylaxis or severe allergy, but they may not be sufficient or applicable to all cases. Therefore, it is advisable to consult a health professional for individualized advice and guidance.

4. BioCeuticals' safety measures for Armaforce

BioCeuticals has implemented several safety measures to reduce the risk of anaphylaxis associated with Armaforce.

Following the TGA's decision to update the label requirements for *Andrographis* in 2020, BioCeuticals added a back-of-pack label warning: “*Andrographis* may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis) or develop any adverse symptoms, stop use and seek immediate medical attention.”

After receiving the fatal anaphylaxis report in June 2024, BioCeuticals immediately implemented a new contraindication label warning. This warning, displayed in a front-of-pack box, states: “Do not use if you have any history of severe allergic reaction. *Andrographis* may cause anaphylaxis. If swelling of the mouth, throat or difficulty breathing occurs, stop use and seek immediate medical attention.” This warning is intended to alert consumers of the potential risk of anaphylaxis and the need for urgent medical attention if they experience signs or symptoms of a severe allergic reaction.

The rationale for the new contraindication label warning is based on [REDACTED], as well as the principles of risk minimisation and consumer protection. The new warning will raise awareness and alertness of the potential risk of anaphylaxis associated with *Andrographis* and will discourage the use of Armaforce in people who are at higher risk of having an allergic reaction.

The new warning will also facilitate the early recognition and prompt treatment of anaphylaxis, which can reduce the morbidity and mortality associated with this serious adverse event. The new warning is aligned with the international regulatory standards and best practices for the

management of anaphylaxis risk, consistent with the established regulatory approach and evidence-based practice for the management of anaphylaxis risk associated with natural health products.

BioCeuticals has also implemented an education plan to inform consumers, health professionals, and retailers of the updated product label and the risk of anaphylaxis associated with Andrographis. The education plan included a letter to health professionals, a Prescribing Decision Tree and product website updates.

BioCeuticals is committed to ensuring the safety of our products and will continue to monitor and manage the benefit-risk balance associated with Armaforce.

Summary of Actions and Benefit-Risk Assessment

In conclusion, BioCeuticals has taken all the necessary actions to mitigate the risk of anaphylaxis associated with Armaforce. BioCeuticals has updated the product label, implemented an education plan, and conducted a comprehensive benefit-risk assessment of Armaforce. The results of this assessment indicate that Armaforce remains a safe and effective product for its intended use and target population, as long as the label warnings are adhered to.

BioCeuticals appreciates the opportunity to provide this information to the TGA and will continue to monitor the safety of Armaforce and report any adverse events as required.

Regards,

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