Technical Alert

TGA outcome of compliance review for *Euphausia superba* (Krill) oil

Dear member,

In April this year, members were informed of the TGA listing compliance review outcomes for medicines containing the ingredient *Euphausia superba* (Krill) Oil. At the time CMA provided information to assist sponsors to conduct a review of indication(s) for Krill oil and to voluntarily make any necessary amendments.

Having given sponsors the opportunity to make voluntary amendments, the TGA will now follow up directly with sponsors of affected medicines. CMA has been advised that the TGA will be targeting the indication concerning 'symptomatic relief of arthritis in only 7 to 14 days'.

From 1 February 2016, the TGA will identify any listed medicines on the ARTG that refer to this indication and initiate a targeted compliance review.

Background:

The listing compliance review found limitations in the provided evidence to support the following indications (please see below for additional detail):

- **Indication**: '*Krill oil can help relieve arthritis symptoms and assist mobility in only 7 to 14 days'*.

Evidence provided: Deutsch L, 2007, Evaluation of the effect of Neptune krill oil on chronic inflammation and arthritic symptoms, *Journal of the American College of Nutrition*, Vol 26(1), pp39-48. Click here.

- **Indication:** 'Krill oil helps support the maintenance of normal LDL:HDL ratio in healthy individuals'.

Evidence provided: Bunea R, El Farrah K, Deutsch L, 2004, Evaluation of the effects of Neptune krill oil on the clinical course of hyperlipidaemia, Alternative medicine review, Vol 9(4). Click here.

Resources:

- Copy of TGA letter template to be sent to individual sponsors which details the actions TGA will undertake.

Review of the Deutsch (2007) study in relation to the claim, 'Krill oil can help relieve arthritis symptoms and assist mobility in only 7 to 14 days'.

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Deutsch (2007) conducted a prospective randomised, double blind, placebo controlled study with a 30 day duration of treatment. The study evaluates the effect of Neptune krill oil (NKO) on C-reactive protein (CRP) in patients with chronic inflammation and also the effectiveness of NKO on arthritic symptoms.

The authors reported a 19.3% reduction in CRP in the NKO treatment group after 7 days of treatment in comparison with an observed increase of 15.7% in CRP reported for the placebo group. In addition, NKO is reported to have shown significant reduction in pain, stiffness and functional impairment.

The TGA evaluation has concluded the following limitations of the Deutsch (2007) study:

- The assessment of the arthritic disease relied on an un-validated WOMAC scale for direct evidence of clinical efficacy.
- The reported results showed inconsistencies in treatment effects:
  - For the pain subscale, a statistically significant change was not observed until day 14.
  - For the stiffness subscale, a statistically significant change was observed at day 7 but not day 14.
  - The functional impairment subscale showed a statistically significant effect at days 7 and 14 but not day 30.
- The two treatment groups in the study comprised patients with cardiovascular disease and/or rheumatoid arthritis and/or osteoarthritis. As CRP may have a different clinical significance in each of these disease states, the reported effect on CRP concentrations cannot be interpreted.
- The study did not address confounding factors such as smoking, obesity and exercise, which may influence the CRP level and hence may contribute to bias.

In summary, the TGA considers that the Deutsch (2007) study does not support the indication '*Krill oil can help relieve arthritis symptoms and assist mobility in only 7 to 14 days'*.

Review of the Bunea (2004) study in relation to the claim: 'Krill oil helps support the maintenance of normal LDL: HDL ratio in healthy individuals'.

Bunea R, El Farrah K and Deutsch L (2004) conducted a multi-centre, three month, prospective, randomised double-blind study to assess the effects of krill oil on total cholesterol, triglycerides, low density lipoprotein (LDL) and high density lipoprotein (HDL).

The TGA evaluation has concluded the following limitations of the Deutsch L (2004) study:

- There are multiple instances of inadequate reporting and multiple errors in reporting.
- As the study was designed to investigate effects of hyperlipidemia, it does not support the claim with respect to healthy individuals. No justification was provided as to why the population of the study is applicable to the different target population of the medicine.

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- In addition, the dosage studied in both Group A (2-3g krill oil, dependent on BMI) and Group C (540mg EPA and 360mg DHA from 3g of fish oil) is far in excess of the dose provided n the evaluated product. Therefore, the recommended dosage of the product is not comparable to the investigated dosage in the study utilised.

In summary, the TGA considers that the Deutsch L (2004) study does not support the indication: '*Krill oil helps support the maintenance of normal LDL:HDL ratio in healthy individuals'*.

Conclusion:
The TGA concludes that the indications for the medicine are not supported by the evidence provided by the sponsor and therefore the certifications made by the sponsor under section 26A(2)(j) of the Act (that the sponsors holds information or evidence to support any claim made in relation to the medicine) are incorrect.

Resources:
- TGA Summary - Krill Oil Evaluation Report
- TGA Evaluation Report – Review of Information and Evidence (redacted)

If you have any questions or require further information please contact Emma Burchell on 02 6260 4022 or email emma.burchell@cmaustralia.org.au

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