Melbourne Dementia Research Centre

Professor Ashley I. Bush
MB BS, DPM, FRANZCP, PhD, FTSE, FAHMS, FAPA
Director, Melbourne Dementia Research Centre

Kenneth Myer Bu d ng
30 Roya Parade, Parkv e
V ctor a 3052 Austra a

P +61 3 9035 6532
F +61 3 9035 5120
ash ey.bush@f orey.edu.au

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Therapeutic Goods Administration
Department of Health,
Australian Government

To whom it may concern,

I write to you as a NHMRC Senior Principal Research Fellow and Director of the Melbourne Dementia Research Centre at The Florey Institute of Neuroscience & Mental Health at the University of Melbourne. I am also a practicing psychiatrist and a highly cited translational neuroscientist with over 440 publications and 29 patents. In 2014 I was awarded the Victoria prize for Science and Innovation and and listed in the World's Most Influential Scientific Minds (Clarivates, 2014-2016, 2018-19). I am a fellow of the Australian Academy of Health and Medical Sciences. Given this extensive experience I sincerely hope you strongly consider my concerns with the 'Proposed clarification that goods are therapeutic goods - goods containing folate substances in certain circumstances.'. In particular, I wish to make the following points in support of Neurofolin remaining as a Food for Special Medical Purposes (FSMP):

- Folate is obtained from the diet. However, a considerable proportion of people have trouble metabolising or processing folate. For these patients, dietary management, including the use of bioactive forms of folate, is critical in helping them maintain health.
- Folate disorders are common in relation to a number of disease states, including those listed in the proposed declaration.
- Products that help patients manage this dietary need are unlikely to be able to be registered as therapeutic products, for several practical reasons that the TGA should already be aware of.
    - Obliging FSMPs to become registered as therapeutic products would increase the barriers of access to products that may be helpful managing dietary aspects related to certain diseases without any additional benefit to public safety.
    - The FSMP framework already requires medical supervision.

- The proposed declaration has a real risk of impacting how some particularly vulnerable patients, those with folate disorders also suffering with treatment resistant depression, manage aspects of their disease related to dietary management.
- The risk of relapse is potentially serious. Many factors can impact the treatment of these patients, including diet. But this does not make dietary management equivalent to a therapeutic.
- The proposal that people currently accessing suitable products in the FSMP category will be able to continue to access them via another means is unlikely to be realised. Non-compliance is high in patients, particularly those with treatment resistant depression. This includes non-therapeutic aspects that may be helpful, such as keeping a healthy diet and exercise. Any additional barrier can disrupt the trajectory of patient care.
- The proposed declaration makes it impossible to have a FSMP containing folate or a derivative of folate for dietary management of patients with folate metabolism disorders, with depression or with both.
    - By extension, sub-populations of patients diagnosed with depression can never have a dietary requirement best handled by a FSMP! This conflicts with a considerable body of evidence that a large proportion of depression patients (up to 70%) may have genetically based impairments in processing normal dietary folate, making a FSMP the most suitable addition to their overall management.
    - Further, the proposed declaration is logically inconsistent with the current legislative framework. FSMPs are explicitly for addressing a dietary need not otherwise addressable with normal food when it relates to a disease or disorder. The proposed declaration undermines the purpose of the legislation defining FSMPs. As FSMPs are not under the regulation of the TGA I am concerned that there appears a push to invalidate the intention and wording of Australia New Zealand Food Standards Code - Standard 2.9.5 which defines FSMPs. If there are objections to the legislated definition and regulations of FSMPs, the TGA should address these at the legislative level rather than attack individual products and uses that are compliant with the FSMP legislation as it currently stands.
- The link between folate and neurotransmitters involved in depression is well established. Folate is a required dietary precursor for the production of

neurotransmitters such as serotonin, norepinephrine and dopamine. This does not make the addition of folate to a patient with deficient folate absorption equivalent to an SSRI or other pharmaceutical any more than it would make amino acid supplements – required for making proteins – a therapeutic.

- I am currently only aware of only one product in Australia that the proposed declaration would affect – Neurofolin – which is produced by a local Australian company.
- Based on the information available, I believe that Neurofolin was designed as a FSMP, following the best available evidence, to help patients manage a dietary requirement for folate when they have an inability to process normal dietary folate, common in many people diagnosed with depression.
- To my knowledge, none of my fellow psychiatrists or our patients believe that Neurofolin can be taken as a cure for depression.
- As a psychiatrist, I do not believe Neurofolin acts in a manner similar to other therapeutics. While I think it achieves the expressed aim of the product, namely, to help management a dietary requirement for folate, it would be inappropriate to force Neurofolin to be regulated as a therapeutic while the FSMP category exists.

Given the above concerns, I sincerely hope that the TGA will reconsider their current pathway and not issue the proposed declaration.

Yours sincerely,

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Professor Ashley Bush