Australian Government

Department of Health

[redacted]
Investigator / Conciliator
Investigation and Conciliation Service
Australian Human Rights Commission
GPO Box 5218
SYDNEY NSW 2001

Dear [redacted]
Thank you for your email of 22 December 2020 asking that the Therapeutic Goods Administration in the Department of Health respond to six questions by 5 February 2021. Your questions and our responses are set out below.

Question One

1. In his complaint, Mr O'Connor states that he has various mental health conditions including depression, anxiety and PTSD. He states he has been using a combination of medications which have been approved for use by the TGA, for the last 8 years to manage these conditions. Mr O'Connor claims that the TGA is required by law to provide Consumer Medicines Information (CMI), including about the multiple life threatening side effects of medications. Mr O'Connor alleges that the TGA's failure to provide such CMI's has breached his human rights. With regard to Mr O'Connor's claims as outlined above, please provide the following information:

    a. Please outline any legislative or regulatory requirements which regulate the content, production and distribution of CMI statements.
    b. Advise whether the TGA approves and/or produces the substantive content included in Consumer Medicines Information (CMI) statements. If the TGA does not have any responsibility for the provision of CMI statements please advise who has such responsibility.
    c. Advise of the nature of TGA's responsibility (if any) for ensuring CMI statements comply with relevant legislation and provide further information in relation to this.

d. Advise of the nature of TGA's responsibility (if any) for the provision or distribution of CMI statements to consumers?

Answer One

The Consumer Medicines Information (CMI) is a leaflet that contains information on the safe and effective use of a prescription medicine, as well as some non-prescription medicines and some biologicals.

The obligation to provide the CMI with each *supply* of a registered medicine which includes a substance entered in Schedules 4, 8 or 9 of the Poisons Standard (the medicines with which Mr O'Connor is concerned) is imposed on the sponsor of the medicine (see regulation 9A(1) read with Part 1 of Schedule 10 of the *Therapeutic Goods Regulations 1990*). Briefly, a schedule 4 substance is a prescription only substance, a schedule 8 substance is a controlled drug and schedule 9 substance is a prohibited substance. In the circumstances of with which we are presently concerned, the responses below focus on obligations pertaining to the CMI for a prescription medicine (a schedule 4 substance).

Relevantly, 'sponsor' in relation to the medicine, means a person who imports or arranges the importation of the medicine into Australia or manufactures the medicine or arranges for another person to manufacture the medicine (see the definition of that term is s 3(1) of the *Therapeutic Goods Act 1989*).

Accordingly, a CMI document is written by the pharmaceutical company (sponsor) responsible for the medicine.

The TGA is not responsible for either the preparation or approval of the CMI document.

A CMI is required, by reg 9A read with Schedule 12 of the Therapeutic Goods Regulations, to include:

- Name of the medicine
- Names of the active and inactive ingredients
- Dosage of the medicine
- What the medicine is used for and how it works
- Warnings and precautions, such as when the medicine should not be taken
- Interactions the medicine might have with food or other medicines
- How to use the medicine properly
- Side effects (as to which, see the response to question two below)
- What to do in the case of an overdose
- How to store the medicine properly
- Name and address of the sponsor
- Date the CMI was last updated

The CMI must also be consistent with the product information (the PI) about the medicine. It is required to be 'written in language that will easily be understood by patients' (see the third and fourth dot points of the first paragraph of Schedule 12 of the Therapeutic Goods Regulations).

The sponsor is also required by reg 9A of the Therapeutic Goods Regulations to make the CMI available to consumers either in the pack or in another manner that will enable the information to be given to the person to whom the medicine is administered or otherwise dispensed. In practice, while the CMI for some medications is provided as a pack insert, for many medications it is available as a supplemental leaflet or for download, to be provided by pharmacists. The TGA is not responsible for the distribution of the CMI.

Through the pharmacovigilance inspection program, the TGA monitors sponsors' compliance with their obligation to submit an updated CMI to the TGA following approval of updates to the Product Information (PI). The nature of this role is informed by the obligation imposed on the sponsor by the Therapeutic Goods Regulations (see regulation 9A read with Schedule 12). Further detail is provided in the response to question two.

Question Two

2. If the TGA does have responsibility and or oversight of the production/approval of CMI Statements, please provide the following information:

    a. Please provide a brief overview of the TGA's involvement in and responsibility for CMI statements.
    b. Please comment on the complainant's allegation that 'the TGA has not ensured the CMI for each medication meets it[s] legal requirement to include (mirror) the same side effects and warnings, in simple and clear language, that exist in the Product Information for that medication.'
    c. If CMI statements are updated, and additional risks are included in a CMI statement, is the TGA responsible for advising consumers of the update?

Answer Two

The CMI is prepared by sponsors based on the PI for their product, and must contain key elements as outlined in response to question one above.

The content of the PI is approved by the TGA as part of the initial registration process for a medicine. Any subsequent changes to the PI after initial approval, whether they are initiated by the sponsor or made at the request of the TGA, must also be approved prior to publication. It is then the sponsor's responsibility to update the CMI accordingly, with it being a condition of registration that updated documents be submitted to the TGA within 2 weeks of the date of approval of the updated PI.

As noted in the answer to question one, the obligation imposed by the Therapeutic Goods Regulations for the content of the CMI is expressed as a requirement to first, be *consistent* with the PI and written in language that will easily be understood by patients (see the third and fourth dot points in the first paragraph of Schedule 12 of the Therapeutic Goods Regulations).

Further, the CMI must describe 'undesirable effects that can occur under normal use of the medicinal product and, if necessary, the action to be taken if experienced. The patient should be expressly invited to communicate any undesirable effect, especially if it is not mentioned in the patient information document, to his or her doctor or pharmacist' (see item 6 of Schedule 12).

It is apparent that 'consistency with the PI' requirement is *not*, as asserted by the complainant, the equivalent of the CMI mirroring 'the same side effects and warnings in simple and clear language that exist in the PI for that medication'. The obligation is that the CMI is compatible with the PI and that it does not contradict it (see the definition of 'consistent' in the *Macquarie Dictionary online*). Further, item 6 of Schedule 12 does not require that the CMI include *all* potential side effects, some of which may be serious, but which are very rare. The CMI must include side effects that can occur with normal use.

Broadly, provided that the CMI covers the matters required by Schedule 12, its exact content is a matter for the sponsor. Accordingly, the combination of the absence of an express role of approval by the TGA of the CMI with the expression of the required inclusions of the CMI means that the TGA does not include in its pharmacovigilance inspections a detailed evaluation and approval of the content of the sponsor's CMI.

In this way, the obligations mandated by the Therapeutic Goods Regulations strike an appropriate risk based balance between ensuring a patient is provided with sufficient information to ensure that the patient takes the medicine prescribed for the treatment or prevention of the relevant illness simultaneously with ensuring that the patient takes appropriate action if they experience a side effect. At a population level, including a long list of adverse events with diminishing probability of risk of occurrence in the CMI diminishes the impact of the warnings for side effects with a higher probability of occurrence.

The required invitation to be in touch with a health practitioner is intended to reduce the risk of patients self-diagnosing any new symptoms that they may experience. There is a clear safety risk to a patient in so doing. The content of the CMI mandated by the Therapeutic Goods Regulations is consistent with the safer course; that would encourage the patient to seek prompt advice from their doctor.

The TGA is not responsible for advising consumers of updates to CMI.

However, it must be noted that, for a significant new risk or side effect to be added to a CMI, it would first have been updated and approved by the TGA for inclusion in the PI and should also have been reported to the TGA by the sponsor (or other healthcare professional etc.) as part of their ongoing pharmacovigilance responsibilities. The TGA has a range of regulatory measures that can be applied in response to the identification of significant safety issues, ranging from communications with the public and/or healthcare professionals (either by the sponsor under direction from the TGA, or by the TGA directly) through to suspension of a product from market and product recalls. Accordingly, the TGA is likely to advise the public of a significant new risk or side effect by means other than revision of a CMI.

Question Three

3. Mr O'Connor also alleges that pharmacists are not providing accurate information on prescription medications and are providing CMI statements that are not up to date. Please advise whether the TGA is responsible for, or does it

have oversight of, pharmacists providing CMI statements and/or medication advice to consumers?

Answer Three

The TGA is not responsible for, nor has oversight of, pharmacists providing up to date CMI statements or medication advice to consumers. The Pharmacy Board of Australia regulates pharmacist practice in Australia.

Question Four

4. With reference to the TGA's role, please comment on Mr O'Connor's allegations that since receiving medical care for physical and mental health conditions since 2012 he has not been provided with the legally required information on all the life-threatening side effects, including drug-drug side effects, of the medications that he has been prescribed.

Answer Four

The PI and CMI documents are important sources of information for patients and healthcare professionals. However, these documents are, by their nature, only general guides to the use of any specific medicine. As such, they should never be regarded as a replacement for individually targeted healthcare advice provided to a patient by their treating doctor.

When a patient starts a new medication it is the responsibility of the prescribing doctor to ensure that the suitability of the medication for that patient has been appropriately considered and any material risks or side effects of treatment have been effectively communicated. This includes consideration of any known drug interactions (readily searchable through a range of reference texts and publically available websites), bearing in mind the patient's current medications and any prior adverse events they may have experienced. This is particularly important if a medicine is prescribed 'off-label'. 'Off label' use occurs when a therapeutic good is used for an indication or intended purpose not specified in the product information or the package label, in a different population to that intended, at a different dose to that recommended, or via a different route of administration. 'Off-label' use is a clinical decision made at the discretion of the prescriber who is responsible for obtaining informed consent from the patient. In the case of 'off- label' use relevant drug interactions may not have been explicitly addressed in the PI or CMI, as these are focussed on the approved indications for use. Pharmacists, when dispensing medications, provide a second source of information about usage and potential risks of those products.

It is not possible to account for all potential drug interactions in CMI, particularly when considering that some patients are prescribed multiple medications, and other patients may experience idiosyncratic drug reactions, i.e. reactions that are unique to that individual and not commonly encountered otherwise. As such, in addition to listing any common or serious known drug interactions, the CMI aims to make clear symptoms that should prompt a patient to seek medical attention and advice.

Question Five

5. Please provide any further information that DOH – TGA considers is relevant to the Commission's inquiry into the complaint.

Answer Five

The TGA is not aware of any other information relevant to the Commission's inquiry which is not set out above and in Adj Prof Skerritt's letter of 23 July 2020, a copy of which is included with the complaint.

Question Six

6. Please advise if DoH-TGA are willing to participate in a conciliation process to try to resolve this complaint.

Answer Six

Yes, the TGA will participate in a conciliation process.

Please be in contact if you would like to discuss our responses.

Yours sincerely

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Principal Legal and Policy Adviser

3 February 2021