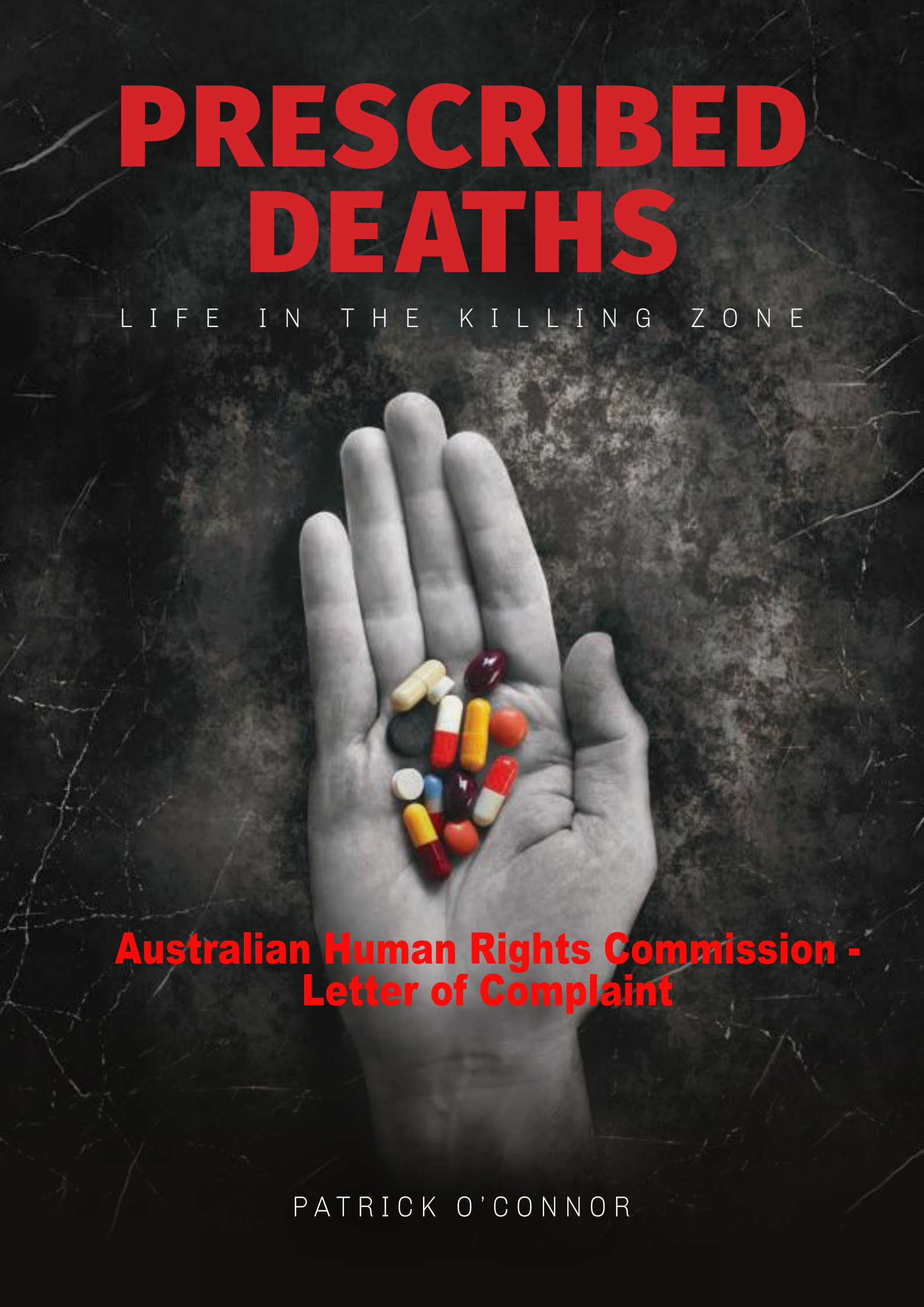
PRESCRIBED DEATHS

LIFE IN THE KILLING ZONE



Australian Human Rights Commission - Letter of Complaint

PATRICK O'CONNOR

Contents

1 Key Points

Key Issue: The consumer warning information that has been provided to me for the medications I have been prescribed, has not contained information on multiple life threatening side effects.

Key Legislation: The *Therapeutic Goods Act 1989* regulates consumer medicine warning information. This complaint will show that not including these side effects is a breach of the legislation and that it has been occurring on a systemic level for over 20 years.

Key Issue: I have not been provided advice or consumer warning information in the majority of the times when pharmacists have dispensed my medication. In some instances advice has been provided that is inaccurate and increased the risk of side effects occurring.

Key Legislation: The *National Health Act 1953* regulates the provision of medicines and Commonwealth agreements with pharmacists also stipulate the legal requirements for consumer medication safety. The failure of pharmacists to uphold these requirements in the provision of medication warnings to me is a breach of ethical and legal commitments.

Key Human Rights: The complaint will argue that the failure to provide accurate and up to date medication information, has breached multiple articles of the CRPD. This includes rights to information, legal capacity, informed consent, abuse and good health.

Commonwealth Department Responsible: Australian Department of Health.

2 Overview

The basis of this complaint is that whilst receiving medical care for physical and mental health conditions since 2012, I have not been provided with the legally required information on all the life threatening side effects of the medications that I have been prescribed. This also includes the drug-drug side effects that occur when medications are combined.

The medication classes I have been prescribed include:

1. Antidepressants
2. Benzodiazepines
3. Opioids
4. Mood stabilisers
5. Antipsychotics
6. Stimulants
7. Hormone replacement therapy
8. Codeine

I have always been prescribed combinations of these medications, as many as seven at any point in time.

The side effects not disclosed in the Consumer Medicines Information (CMI) include:

- Death
- Addiction
- Dependence
- Tolerance
- Withdrawal syndrome
- Overdose

- Respiratory depression
- Abuse
- Medicine interaction
- Alcohol interaction
- Coma

These medications are scheduled drugs due to these exact side effect risks.

The failure to provided me with this information in the CMI documents has exposed me to significant side effect risks, many I have suffered from and increased the risk of suicide to myself.

The regulation of the CMI is the responsibility of the Therapeutic Goods Administration (TGA). The *Therapeutic Goods Act 1989* provides the legal requirements for patient information documents. This complaint will detail how pharmaceutical companies have breached TGA regulations by deliberately withholding information that is legally required to be included in the CMI. Primarily this is information on the life threatening side effects.

Reports from the ABS, AIHW, Department of Health, Penington Institute, and the National Drug and Alcohol Research Centre, also show that the medications I have been prescribed and the exact risks not disclosed, are directly or indirectly linked to the majority of Australia's adverse drugs events – hospitalisations, suicides and deaths – over the last 20 years.

Whilst this complaint is about my personal experiences, I am fortunate to not be one of the thousands of Australians who are no longer alive to make a complaint.

The rights of vulnerable people – in fact, all people – to safe healthcare is enshrined in the Universal Declaration of Human Rights, the Australian Charter of Healthcare Rights, and the Convention on the Rights of Persons with Disabilities. It is a legal requirement that people are provided with accurate, up-to-date information on the risks of all medications. This includes when multiple medications are prescribed.

The TGA has failed to uphold the rights of persons with disabilities to information, which impacts our ability to exercise our legal right to informed consent and most tragically fails to uphold our right to the highest attainable standard of health. You simply cannot assess a risk that you don't know about. You cannot follow safety advice if it has never been given to you.

Pharmacists have ethical and legal requirements for the provision of the CMI and verbal advice to consumers. The Seventh Community Pharmacy Agreement (7CPA) is an agreement between the Commonwealth Government, the Pharmacy Guild of Australia (The Guild) and the Pharmaceutical Society of Australia (PSA). This agreement outlines the responsibilities of pharmacists in delivering medication Information to consumers. This complaint will show how pharmacists have failed to meet these obligations in my interactions with them.

The outcome I am seeking can be summarised into 4 areas:

- Urgent action is required to update all relevant CMIs and to ensure all existing users of these medications are made aware of the risks not previously disclosed
- The TGA to commence approving all CMIs before they are made available to consumers
- Acknowledgement of the retrospective breaches and action taken against the companies responsible
- Pharmacists are policed to ensure they deliver their obligations to provide advice and the CMI to consumers

3 Prescribed Deaths – Life in The Killing Zone

My personal experiences with the healthcare system was the driving force behind the report I have submitted titled *Prescribed Deaths – Life in the Killing Zone* (PDLKZ). In this complaint I will reference the relevant sections of the report, and other supplementary documents that are products of submitting this report to government bodies.

The *Prescribed Deaths – Life in the Killing Zone* documents systemic issues that exist in the treatment of mental health and pain conditions. The report was produced focusing on industry wide issues, but these are issues that I am aware of as they have personally impacted me. To validate my report, it has been independently reviewed by experts in Australia and the US. There is no question that systemic discrimination and human rights breaches have occurred, and still do, and I have experienced these personally.

4 Legal Accountability

The Australian Government Department of Health is responsible for the regulation of the health and aged care system to protect Australians health and safety. They are also responsible for funding Australia's health systems, such as Medicare and the Pharmaceutical Benefits Scheme (PBS).

The TGA regulates consumer warning documents for prescription medication in Australia. The TGA is part of the Australian Government Department of Health, and is responsible for regulating therapeutic goods including prescription medicines, vaccines, sunscreens, vitamins and minerals, medical devices, blood and blood products.

The Australian government endorses the CMI as the information source for accurate medication safety and side effects, including prescription medication interactions. Approving these medications for the PBS provides a further endorsement in the minds of Australians – given the PBS subsidises the cost, it makes the medication more accessible to us.

However, the TGA has no approval process for the content of each CMI, especially the side effects. The Australian Department of Health and the TGA endorse a document, which Australians trust to protect them from medication deaths, that has not been reviewed and formally approved by the TGA.

The failure to ensure that vulnerable people are provided with accurate information is not only a breach of our right to safe health care, it also means that the government has full culpability for the failings and the resulting health issues we have suffered.

The 7CPA details the obligations of pharmacists in the provision of consumer warnings. This agreement is overseen by the Australian Government Department of Health.

The Australian Government, through the Department of Health, has overseen these healthcare system failures. Responsibility for the safety of the healthcare system rests with them.

<u>More Information:</u>

PDLKZ: Chapters Two, Four, Five, Six, Nine, Eleven

5 Therapeutic Goods Act 1989

The role of the TGA is to ensure all Australians are provided with the highest level of medication safety. *Chapter Two: Consumer Warnings* of *Prescribed Deaths – Life in the Killing Zone* details the role of the TGA and the regulations they oversee. The central failing is that the TGA has not ensured the CMI for each medication meets it 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. In addition, my complaint will detail how medically acknowledged risks and side effects, known to the TGA and the Dept of Health, have not been included in the CMIs. This information is detailed in industry updates and government websites, yet they have failed to ensure it is present in the CMIs.

2.1 PRODUCT INFORMATION – THE SCIENTIFIC GUIDE

*The **Product Information (PI)** for all prescription medications:*

provides health professionals with a summary of the essential scientific information for the safe and effective use of a prescription medicine. The information has been written by the pharmaceutical company responsible for the medicine and has been approved by the TGA. It provides objective information about the medicine's quality, safety and effectiveness, as demonstrated in the data provided to the TGA by the pharmaceutical company.

2.2 CMIS – THE CONSUMER GUIDE

*The document that is designed for consumers is called the **Consumer Medicines Information (CMI)**:*

The information has been written for consumers by the pharmaceutical company responsible for the medicine. It provides information on the safe and effective use of a prescription medicine. CMIs are important to consumers and those who provide medicines and care, as they provide information aimed at bringing about better health outcomes.

While the PI is approved by the TGA, the CMI is not. The TGA admits that they have no procedure to assess and approve the content of each CMI, however the *Therapeutic Goods Regulations 1990* requires the CMI to be consistent with the PI. In the analysis that I have undertaken, the research is focused on the serious side effects and warnings of each medication. I focus on information that is contained in the PI and compare that to the information in the CMI. The report then details the information that has not been included in the CMI or information that is inaccurate, misleading, or incomplete.

The TGA is responsible for enforcing the *Therapeutic Goods Regulations 1990.*[1] The Statutory Rules No. 394, 1990 made under the *Therapeutic Goods Act 1989,* Schedule 12—Patient information documents (subregulation 9A(1)), requires the TGA to enforce the legal requirement that the CMI is consistent with the PI.

The TGA must also ensure that information in the CMI meets the requirements as per the 'Patient information documents' section of the Act. Schedule 12 of the *Therapeutic Goods Regulations 1990* states that a CMI must include information on contraindications, precautions for use, interactions with other medicines and alcohol, special warnings, withdrawal or other adverse effects, habit forming potential, symptoms of overdose, and undesirable/unwanted effects that can occur. My complaint also includes information that is relevant to these areas, that is acknowledged by the TGA and the Department of Health.

[1] Australian Government, Therapeutic Goods Regulations 1990, Compilation No. 94, 1 July 2020.

The TGA's 2018 opioid consultation paper titled *Prescription strong (Schedule 8) opioid use and misuse in Australia – options for a regulatory response* clearly demonstrated that the TGA's role and powers under the *Therapeutic Goods Act 1989* include the ability to require information in the PI to be included in a CMI. While the TGA does not have a role to approve each CMI, it has a clear role to ensure CMIs meet the legal requirements, with the ability to change the content.

The TGA states in the paper, *While the TGA does not approve the CMI it should mirror the information in the PI, therefore ensuring the PI has the correct information about the risks and appropriate use of opioids would ensure it was mirrored in the CMI. Work is necessary to make sure the CMI remains consistent with the PI, as is currently required,…*

The report and my complaint focuses on the core role of the CMI to provide information on the risks associated with taking a medication. The Act requires details of these risks be included under the following areas:

- 3 Advice before using the medicinal product (e.g. interactions like alcohol or other medications, special warnings)
- 4 How to use the medicinal product properly (e.g. withdrawal or other adverse effects)
- 5 Further information (e.g. habit forming)
- 6 Unwanted effects
- 7 In case of overdose (e.g. symptoms and emergency procedures)

In the analysis that I have undertaken, I focus on these areas of Schedule 12 of the Act and compare the information that is contained in the PI and compare that to the information in the CMI. I also provide other TGA and Dept of Health references for these risks to further highlight the known medication risks not present in the CMIs.

More Information:

PDLKZ:
- Chapter Two

6 Medical Diagnosis – Patrick O'Connor

In 2012 I was diagnosed with depression and anxiety by my regular GP. Since that time I have received continuous medical care from various GP's, psychiatrists and psychologists. My diagnosis's are Major Depressive Disorder, Post Traumatic Stress Disorder, and Anxiety Disorder. My conditions are classed as severe and treatment resistant.

My conditions have been treated with psychological and pharmacological treatments. The medication prescribed to me commenced in 2012 and continues today. It has involved dozens of prescribed medications, both on and off label. I have always been prescribed polydrug treatments, meaning that I have always been prescribed at least two and as many as seven medications, at the same time.

The complexity of my illnesses and the lack of response to medication, required a significant focus on adjusting the medications prescribed. This has not only resulted in numerous medications being trialled, but also multiple combinations of medications being prescribed in an effort to produce of a polydrug combination that would deliver therapeutic benefits.

The number of different medications, combinations of medications and doses, is approx. 250. The number of visits to pharmacies is approximately 200.

I have a long history of alcohol use and abuse, which was diagnosed as a form of self-medication. This was present before my diagnosis, and for a number of years post diagnosis. I have provided some medical history from mental health physicians to this complaint.

People with mental illnesses have a higher risk of death by suicide. Due to the inability to achieve an improvement in my mental illness, for large periods of the last 8 years I have experienced feelings of suicidal ideation. On 2 occasions I have attempted to end my own life using the medication that I have been prescribed. Fortunately I am now in a more stable period of improved mental health, thanks to the treatments that I have been able to access in the USA.

I also have a rare hormone condition known as Kallmann's Syndrome (Hypogonadism), which manifests as low testosterone. This is treated with Hormone Replacement Therapy (HRT), which involves testosterone injections. I have provided some medical history from physicians to this complaint.

In 2017 I began travelling to the US for treatments for mental illness and low testosterone that are not available in Australia. It was during these visits that I became aware of the consumer warnings given to patients for medications in the US. This alerted me to the information that is not present in Australian CMIs for the same medication, made by the same companies.

I also have Severe Sleep apnoea, which is treated with CPAP.

I have a number of physical injuries, including long term pain and restricted movement in my left knee. These have required multiple operations and pain management with medication.

More Information:

PDLKZ: About The Author - Patrick O'Connor

7 Medications Prescribed – Patrick O'Connor

Severe mental illness rarely exists as a single condition and sufferers like me typically deal with multiple chronic illnesses. To attempt to improve our afflictions we are managed by multiple doctors, using complex medication prescriptions combined with other treatments. Chronic pain is a condition commonly present in people with mental illness. These are both medical conditions that medication is the most common form of treatment.

The following is a summary of the majority of the medications that I have been prescribed since 2012. Bold medications are specifically analysed in the *Prescribed Deaths – Life in the Killing Zone* report.

7.1 Mental Health Medication

1. **Efexor XR** (Antidepressant)
2. **Fluoxetine** (Antidepressant)
3. Mirtazapine (Antidepressant)
4. Ciprimil (Antidepressant)

5. Ativan (Benzodiazepine)
6. **Valium** (Benzodiazepine)

7. **Lithium Carbonate** (Mood Stabiliser)
8. Lamotrigine (Mood Stabiliser)
9. Risperdal (Antipsychotic)
10. Abilify (Antipsychotic)

11. **Dexamphetamine** (Stimulant)
12. Vyvanse (Stimulant)

13. Prazosin (Alpha blocker)
14. Propranolol (Beta blocker)

15. Circadin (Melatonin)

16. Duromine (Anorectic agent)

7.2 Pain Medication

1. **Endone** (Opioid)
2. **Panadeine Forte** (Codeine)
3. **Nurofen Plus** (Codeine)

7.3 Hormone Replacement Therapy Medication

1. Reandron (Testosterone enanthate)
2. Sustanon 250 (Testosterone enanthate)
3. Primoteston (Testosterone enanthate)
4. Anastrozole (Non-steroidal aromatase inhibitors)

7.4 Polydrug Combinations

Polydrug medication prescriptions have been a consistent part of my treatment. I have always been prescribed two and as many as seven medications at any point in time. Many additional risks develop when prescription medications are taken together. In addition to these medications I have also experienced periods of alcohol use, sometimes excessive, which is an additional drug interaction risk.

Some of the polydrug combinations include:

1. Efexor XR, Lithium Carbonate, Valium, Lamotrigine, Sustanon 250
2. Fluoxetine, Mirtazapine, Valium, Reandron, Panadeine Forte
3. Fluoxetine, Efexor XR, Valium, Duromine
4. Efexor XR, Mirtazapine, Valium, Propranolol, Panadeine Forte, Dexamphetamine
5. Vyvanse, Endone, Panadeine Forte, Valium, Primoteston, Circadin, Anastrozole
6. Endone, Efexor XR, Valium, Dexamphetamine, Primoteston, Anastrozole

More Information:

PDLKZ: Chapters One, Two, Three, Eleven

8 CMI vs PI risks and warnings

The following tables provides some examples from the *Prescribed Deaths – Life in the Killing Zone* report, of risks that have been deliberately withheld from the CMIs for medications I have been prescribed.

Medication	Manufacturer	PI vs CMI Analysis
Dexamphetamine	Aspen	The CMI states that using this medicine strictly as your doctor prescribed will ensure that abuse or drug dependence should not be a problem. The PI states that dependence and death can occur at prescribed doses.
Dexamphetamine	Aspen	The CMI also does not contain the PI risks of death from using the medication at usual doses or from an overdose.
Valium	Roche	The risks noted in the Valium PI but not the CMI include abuse, withdrawal syndrome, suicidal thoughts, fatal risks if combined with alcohol, and death.
Valium	Roche	The Valium PI also contains multiple warnings in relation to using a benzodiazepine with opioids – the leading cause of drug deaths in Australia. It states that the combined use should be avoided. It advises to prescribe the lowest dose for the shortest period of time if used together. It warns of the risk of overdose, respiratory depression, sedation, coma and death. The CMI does not even mention opioids once, nor these associated risks and warnings.
Valium	Roche	The PI states the risk of combining Valium with antidepressants includes severe sedation, coma, death, respiratory and cardiovascular depression. The CMI simply states that Valium may affect how well other medications work.
Panadeine Forte	Sanofi-Aventis	The CMI from 2000-2020 did not contain a single mention of the risk of death, addiction, dependence, tolerance, withdrawal or abuse. It contains no mention of the side effects of using the medication with alcohol or benzodiazepines. In total, we identified 14 areas as breaches of the *Therapeutic Goods Act 1989*.
Panadeine Forte	Sanofi-Aventis	The CMI does not include that the risk of addiction is increased in patients with a mental illness. It also does not mention that the risk of addiction also increases the longer the drug is used and with higher doses.
Efexor XR	Pfizer	The CMI does not include the life-threatening risk of serotonin syndrome, nor does it warn of the risk of death from an overdose. It also does not include the warning that prescriptions should be written for the

		smallest quantity of medicine in order to reduce the risk of overdose.
Lithium Carbonate	Aspen	The Lithium CMI does not include the PI warning that lithium toxicity can result in coma and death. It also does not include the PI warnings that lithium toxicity can happen at prescribed doses, nor the risk of death from an overdose.
Endone	Aspen	The Endone CMI describes the side effect of consuming alcohol whilst taking the medication as dizziness. In the PI provided to doctors, the side effects listed include profound sedation, coma and death.
Endone	Aspen	The CMI provides no information on the recommended use of Endone, it does not state that it is an opioid or that death can occur at therapeutic doses.
All content can be found in chapter two, except Panadeine Forte which is in chapter three and Patrick O'Connor, Professor Skerritt TGA Letter of Reply, 4th August 2020.		

8.1 Polydrug Risks

The life threatening risks of combining antidepressants, benzodiazepines, mood stabilisers, antipsychotics, opioids and codeine medications is detailed in the *Prescribed Deaths – Life in the Killing Zone* report. When these medications are used together, the risks multiply – particularly the risk of death.

The leading cause of drug deaths in Australia is taking an opioid and a benzodiazepine. The risk of death is 15 times greater than that for a person not taking these medications, which occurs even at prescribed doses. Neither consumer warning for either medication class has included this information for 20 years. This is evidenced by the Valium and Endone CMIs. Neither medication even mentions the other medication class or the fatal risks of this combination.

The report also details how alcohol provides a deadly additional drug to these medications and combinations of medications, yet the lethal side effect risks are also not included in the CMIs.

After a review in 2018, the TGA in 2020 requires opioid CMIs including Endone, to include the warning that combining them with other medications like benzodiazepines, other pain relievers, antidepressants, and antipsychotics, may result in severe drowsiness, decreased awareness, breathing problems, coma and death. These are all warnings that have been present in the PIs for decades. Unfortunately, these warnings are not present in the non-opioid CMIs (benzodiazepines, other pain relievers, antidepressants, and antipsychotics) and the TGA has not indicated if they will ever be added.

It is clear that the polydrug risks of my treatment was almost non-existent in the CMIs of the medication I was prescribed. These are risks are that well detailed in the PIs for these medications.

8.2 Additional breaches for CMI content

The report identifies multiple instances where CMI information is deliberately misleading, inaccurate or incomplete. These are also a breach of the 'Patient information documents' (subregulation 9A(1)) section of the Act. For example:

- The Endone CMI states, 'If abused it may become less able to reduce pain.' Endone is a Schedule 8 drug due to the risk of addiction, abuse and death. This warning completely fails to provide the TGA's position on the risks associated with abuse to the consumer.
- Valium (Diazepam) is another scheduled drug due to the risk of addiction, yet the CMI does not once mention the risk of addiction. Benzodiazepine addiction is a well acknowledged risk; even the government's healthdirect website states, 'If used over a long period, you can become addicted to diazepam.'[2] As far back as 1991, Australia's top medical authority, the National Health and Medical Research Council, issued a warning that benzodiazepines should only be used for short periods as there was a high risk of addiction, and a serious withdrawal syndrome after long-term use.[3]

The Victorian Government Health website states that *Benzodiazepines are highly addictive and should only be used under supervision of a doctor*.[4]

In 2018 the Healthdirect website published an article titled *Prescription addiction can happen to anyone* which stated that *many patients are unaware that prescription medications such as opioids and benzodiazepines can be highly addictive and dangerous to use long term*[5] The reason patients are not aware of the risk of benzodiazepine addiction is that the CMI doesn't contain this warning!

The TGA has a responsibility to not only ensure that the content of the CMI is consistent with the PI, they also must ensure that all content in the CMI is accurate and provides the information that is required under the Act.

More Information:

- PDLKZ: Chapters One, Two, Three, Four, Five, Seven, Eleven
- Patrick O'Connor, Professor Skerritt TGA Letter of Reply, 4th August 2020
- Patrick O'Connor, Professor Skerritt TGA Letter, 1st November 2020

9 New research - additional risks not in the CMI

For this human rights complaint I have included information on risks of medications that I have been prescribed, that was not included in the *Prescribed Deaths – Life in the Killing Zone* report. The medications analysed are relevant to my personal situation as they are medications I have been prescribed or are currently prescribed. This analysis includes information on inconsistencies between the CMI vs PI and information that the TGA made public in updates yet was not included in the CMI.

[2] healthdirect website, accessed on 28 July 2020, see https://www.healthdirect.gov.au/diazepam
[3] https://www.theage.com.au/national/accidental-addicts-20030616-gdvvx8.html
[4] https://www.betterhealth.vic.gov.au/health/healthyliving/tranquillisers
[5] https://www.healthdirect.gov.au/blog/prescription-medicine-addiction-can-happen-to-anyone

9.1 Lithium Carbonate

The TGA Medicines Safety Update Volume 8, Number 4, August-September 2017[6] discussed risks of Lithium Carbonate that have been not included in the CMI.

Health professionals are reminded that early symptoms of lithium toxicity can occur close to or within the serum therapeutic range. You should remain vigilant for potential signs of lithium toxicity, particularly in patients with risk factors.

The risk of lithium toxicity is adequately addressed in the Product Information for Quilonum SR and Lithicarb

There are relatively narrow margins between therapeutic and toxic dosages for lithium and therefore regular blood and clinical monitoring is important. In addition, toxicity occurring close to or within the target serum lithium concentration range is a known risk. Failure to recognise the early signs of toxicity may lead to a delay in treatment and result in poor patient outcomes including, in the worst cases, death.

The most important site of toxicity is the central nervous system. Neurological manifestations of lithium intoxication such as ataxia, dysarthria, dysphagia and cognitive impairment may not be fully reversible despite appropriate treatment. Severe toxicity may result in convulsions, myoclonus and coma.

9.2 Propranolol

In September 2014 Professor John Skerritt replied to Mr Josh Munro, Coroners Registrar, Coroners Court of Victoria regarding Propranolol[7]. Professor Skerritt advised Mr Munro that he would publish an article that advises health professionals to exercise caution when prescribing Propranolol to patients suspected of being at risk of self-harm, particularly by overdose. The article also advises of recorded overdoses and deaths due to Propranolol and states:

Overdosage of propranolol can result in bradycardia, hypotension, bronchospasm and/or acute cardiac failure.

If propranolol is prescribed, consider providing prescriptions for smaller quantities or make other arrangements to reduce the amount of the drug that the patient has access to at one time.

The risks included in the article and the risk of death is not included in the Apotex Propranolol August 2018 CMI[8]:

9.3 Valium

The following risks are included in the Roche Valium January 2020 PI but not in the Roche Valium CMI March 2018:

The risk of dependence increases with dose and duration of treatment.

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[6] https://www.tga.gov.au/publication-issue/medicines-safety-update-volume-8-number-4-august-september-2017

[7] https://www.coronerscourt.vic.gov.au/sites/default/files/2018-12/response%2Btherapeutic%2Bgoods%2Badministration_webster.pdf

[8] Apotex Propranolol August 2018 CMI

After as little as one week of therapy, withdrawal symptoms can appear following the cessation of recommended doses (e.g. rebound insomnia following cessation of a hypnotic benzodiazepine).

Following the prolonged use of Valium at therapeutic doses, withdrawal from the medication should be gradual. An individualised withdrawal timetable needs to be planned for each patient in whom dependence is known or suspected. Periods from 4 weeks to 4 months have been suggested.

Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol, have occurred once physical dependence to benzodiazepines has developed or following abrupt discontinuation of benzodiazepines. They may consist of headache, diarrhoea, muscle pain, insomnia, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases, the following symptoms may occur: dysphoria, palpitations, panic attacks, vertigo, myoclonus, akinesia, hypersensitivity to light, sound and touch, abnormal body sensations (e.g. feeling of motion, metallic taste), depersonalisation, derealisation, delusional beliefs, hyperreflexia and loss of short term memory, to a major syndrome which may include convulsions, tremor, abdominal and muscle cramps, confusional state, delirium, hallucinations, hyperthermia, psychosis, vomiting and sweating.

The failure of the TGA to ensure CMIs contain the required information is highlighted in the analysis of benzodiazepine CMIs including Valium, in my letter to Professor Skerritt on the 1st of November 2020. This letter details multiple risks known to the TGA and the Dept of Health, that have not been included in the Valium CMI. This letter details the failure of the TGA to take action to have these risks added, following a Victorian coroner's inquest in 2012, a TGA benzodiazepine review in 2014, US FDA warning additions in 2016 and 2018, as well as following the TGA opioid review in 2018.

9.4 Vyvanse

The following risks are included in the Shire Vyvanse April 2020 PI[9] but not in the Shire Vyvanse January 2018 CMI[10]:

Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses.

Careful supervision is required during withdrawal from abusive use since severe depression may occur.

Serotonin syndrome can occur in association with the use of amphetamines such as VYVANSE, when given in conjunction with serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs).

Fatal poisoning is usually preceded by convulsions and coma.

The Shire Vyvanse January 2018 CMI states:

Like all stimulants, VYVANSE may become habit-forming and can be abused by some people. If it is taken correctly as instructed by your doctor, this should not happen, either now or later in life.

[9] Shire Vyvanse April 2020 PI
[10] Shire Vyvanse January 2018 CMI

This statement is not included in the Vyvanse PI and is inconsistent with Australian government warnings on amphetamines. Vyvanse is also a 'Schedule 8 drugs - Drugs of addiction' in NSW, yet addiction is not mentioned in the CMI.

The Shire (US) Vyvanse Prescribing Information January 2018[11] also contains information that is not available in the Australian CMI:

CNS stimulants (amphetamines and methylphenidate-containing products), including VYVANSE, have a high potential for abuse and dependence.

Individual patient response to amphetamines varies widely. Toxic symptoms may occur idiosyncratically at low doses.

Advise patients that there is a potential serious cardiovascular risk including sudden death, myocardial infarction, stroke, and hypertension with VYVANSE use.

This is information that the TGA has access to and raises questions as to why it is not in the Australian PI and CMI.

9.5 Duromine

The following risks are included in the iNova Duromine September 2018 PI[12] but not the iNova Duromine September 2018 CMI[13]:

Overdose

cardiac arrhythmias, convulsions, fatigue, central nervous system depression and coma. Cardiovascular consequences include hypertension, hypotension and circulatory collapse.

9.6 Efexor XR

The following risks are included in the Pfizer Efexor XR September 2019 PI but not the Pfizer Efexor XR September 2019 CMI:

However, there have been reports of venlafaxine interaction with lithium resulting in increased lithium levels.

9.7 Lamotrigine

The Aspen Lamictal (Lamotrigine) 2013 CMI[14] warns that:

Anti-epileptic medicines such as Lamictal may increase the risk of suicidal behaviour (including suicidal thoughts and suicide attempts).

However it did not include the warning of fatal overdoses that was detailed in the Aspen Lamictal 2012 PI[15]. I was prescribed Lamotrigine in 2014-2015.

[11] Shire (US) Vyvanse Prescribing Information January 2018
[12] iNova Duromine September 2018 PI
[13] iNova Duromine September 2018 CMI
[14] Aspen Lamictal (Lamotrigine) 2013 CMI
[15] Aspen Lamictal 2012 PI

The Aspen Lamictal 2018 CMI[16] has been updated and does contain this warning:

If you take too much Lamictal you may be more likely to have serious side effects which may be fatal.

9.8 Serotonin Syndrome

SSRI stands for Selective Serotonin Reuptake Inhibitor. SSRI antidepressants are a type of antidepressant that work by increasing levels of serotonin within the brain. Efexor XR is an SSRI. Serotonin syndrome is a toxic state caused mainly by excess serotonin within the central nervous system. It results in a variety of mental, autonomic and neuromuscular changes, which can range in severity from mild to life-threatening. The CMIs for Efexor XR (Venlafaxine) and Lithium Carbonate do not mention serotonin syndrome, yet it is included as a risk in the PIs for both medications.

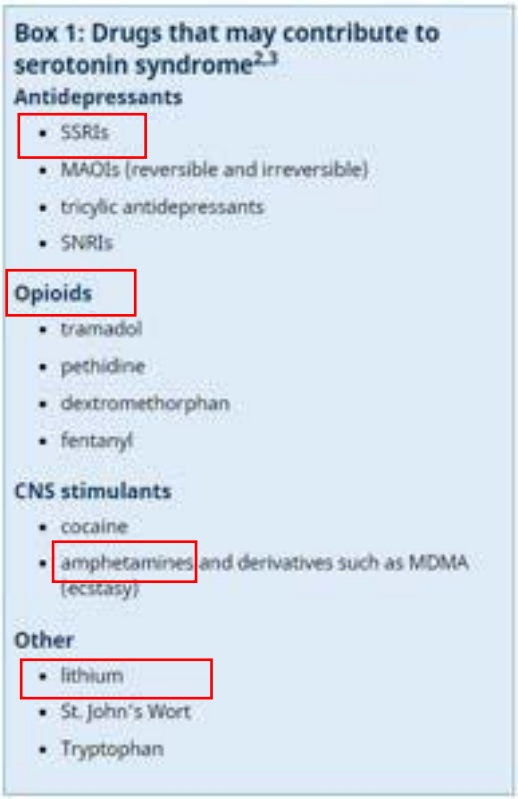
The TGA September 2014 Safety advisory - risk of serotonin syndrome[17] states:

In some cases serotonin syndrome can lead to loss of consciousness, coma and death.

The TGA Medicines December 2010 Safety Update No.6[18] states:

Serotonin syndrome: a reminder

Concomitant use of serotonergic drugs, or use of a single agent in a susceptible patient, can lead to serotonin syndrome which can be life-threatening.



Box 1: Drugs that may contribute to serotonin syndrome[2,3]

Antidepressants

- SSRIs
- MAOIs (reversible and irreversible)
- tricyclic antidepressants
- SNRIs

Opioids

- tramadol
- pethidine
- dextromethorphan
- fentanyl

CNS stimulants

- cocaine
- amphetamines and derivatives such as MDMA (ecstasy)

Other

- lithium
- St. John's Wort
- Tryptophan

[16] Aspen Lamictal 2018 CMI
[17] https://www.tga.gov.au/alert/serotonin-blocking-medicines-used-treat-nausea-and-vomiting
[18] https://www.tga.gov.au/publication-issue/medicines-safety-update-no6-2010

The TGA Australian Adverse Drug Reactions Bulletin, Vol 23, No 1 February 2004[19]

The syndrome often occurs within a day of a change in treatment (increase in dose or addition of another serotonergic agent) and the evolution of symptoms is rapid.

Health professionals should note the drugs that may cause serotonin syndrome, alone or in combination with other serotonergic agents, and be alert to the features of serotonin syndrome. Patients should be informed of the risk and symptoms of serotonin syndrome when serotonergic agents are prescribed.

Table 1: Agents causing serotonin syndrome

Antidepressants	SSRIs, monoamine oxidase inhibitors (including moclobemide), tricyclics, mirtazapine, venlafaxine
Antiparkinsonians	Amantadine, bromocriptine, levodopa, selegiline, carbergoline, pergolide
Illicit drugs	Cocaine, hallucinogenic amphetamines such as MDMA (ecstasy), LSD, etc.
Migraine therapy	Dihydroergotamine, naratriptan, sumatriptan, zolmitriptan
Other agents	Tramadol, carbamazepine, lithium, reserpine, sibutramine, St. John's wort, bupropion, pethidine, morphine

ADRAC has received 161 reports of serotonin syndrome. The majority describe the syndrome in association with the concomitant use of 2 or more serotonergic agents, in particular SSRIs (68), tramadol (29), moclobemide (23), venlafaxine (18), tricyclic antidepressants (18) and St John's wort (8). In 61 reports, the serotonin syndrome developed in association with a single agent: SSRIs (40), moclobemide (5), venlafaxine (5) and tramadol (5).

These are other examples of the TGA being aware of a side effect risk of a medication, yet not ensuring this risk has been disclosed in the CMI.

This information combined with the information contained in the report, provides a comprehensive analysis of the risks that I have been exposed to without the legally required warnings in the CMI. This also demonstrates that the TGA has been aware of these risks, but has failed in its duty to ensure they are also included in the CMI.

10 Adverse Drug Events and Death

Chapter three of the *Prescribed Deaths – Life in the Killing Zone* report details that the classes of medication that has been prescribed to me, are also the leading cause of drug deaths and hospitalisation in Australia. The victims are most commonly people who are taking medications that are prescribed by their own doctor, for diagnosed mental illness and pain conditions, with medications dispensed by their usual pharmacist. The number of deaths has trebled since 2007 and it continues to rise each year.

The most common class of drug identified in toxicology reports in drug-induced deaths are opioids. Opioids (including prescription use) have been the leading class of drug deaths for the last 20 years. Depressants, which include benzodiazepines, have consistently been the second most common class of drug, with antidepressants the third most common present in drug-induced deaths. Deaths due to antipsychotics has also been increasing markedly since 2013.

[19] https://www.tga.gov.au/publication-issue/australian-adverse-drug-reactions-bulletin-vol-23-no-1

The polydrug risks are also well documented. In 2017 the Australian Bureau of Statistics (ABS) Director of Health and Vital Statistics, James Eynstone-Hinkins, said drug deaths were most commonly associated with benzodiazepines and oxycodone, noting that, “These are both prescription drugs which are used to manage anxiety and pain respectively”. The report provides other information on polydrug deaths and hospitalisation.

People with mental illness typically live between 10 and 32 years less than the general population and it is the medication prescribed which is identified as the leading cause. The risks that I have been exposed to are life threatening and have resulted in thousands of Australian deaths. Tragically these warnings are well known to the TGA, but not consumers.

More Information:

- PDLKZ: Chapters One, Two, Three, Four, Five, Six, Seven, Ten, Eleven
- Patrick O’Connor, Professor Skerritt TGA Letter of Reply, 4th August 2020
- Patrick O’Connor, Professor Skerritt TGA Letter, 1st November 2020

11 Off Label Prescriptions

A number of medications I have been prescribed are classed as ‘off-label’. Using a medication off-label means a person is being prescribed a drug for a medical condition that the drug was not designed or tested for. In these instances the CMI will not contain any additional risk that applies to its use ‘off-label’.

For example the prescription of Dexamphetamine is due to my extreme fatigue and exhaustion caused by my PTSD. Dexamphetamine is a stimulant and provides a medication to reduce my feelings of low energy. However it has not been tested by the manufacturer for this use, and the risks of its use for my condition are not included in the CMI.

Examples of medication I have been prescribed off-label include Dexamphetamine, Lithium Carbonate, Propranolol and Lamotrigine. As the CMIs will not contain any information on the risks for off-label use to the person. This means that even if I received a CMI, it will not meet the information requirements for informed consent. The Dept of Health allows the practice of medications being prescribed ‘off-label’ but it does not ensure consumers have access to information on the associated risks of using the medication ‘off-label’.

More Information:

- PDLKZ: Chapters Three, Five, Thirteen

12 Lethal Means of Death

Chapter Eleven details the statistics from the last 20 years that the medication prescribed to treat mental illness and pain conditions are also the same medications used in suicide attempts and deaths. This includes benzodiazepines, antidepressants, opioids, analgesics and antipsychotics. These medications, and polydrug combinations of medications like opioids and benzodiazepines, are toxic enough to be classified as a lethal means of death.

The most common source of these medications is a person’s usual doctor. It is common for these medications to be prescribed to a person who is at increased risk of self-harm, like myself. However, the CMIs for medications contain almost no information on the risk of

medications being used in self-harm or suicides, nor does it provide any safety information that can be taken to reduce this risk.

For example, the Prozac PI (2020) states:

During a 13-year period, there were 34 fatal reports of overdose where fluoxetine was the only reported ingestant.

On the management of suicide risk, the PI states:

Prescriptions for PROZAC should be written for the smallest quantity of medicine consistent with good patient management, in order to reduce the risk of overdose.

The Prozac CMI (2019) provides no warning of the risk of death from an overdose, and no warning to limit access to the medication supplies to prevent suicide attempts from an overdose.

The *Prescribed Deaths – Life in the Killing Zone* report details measures recommended by the WHO on high-risk medication, including having a family member store medications safely and dispense safe quantities as necessary – for instance keeping medication in a locked cabinet and only filling smaller prescription quantities at pharmacies. Reducing access to lethal means in the home, such as firearms and medication, can determine whether a person at risk for suicide lives or dies. The WHO also state that having lethal prescription medications in the possession of a person actually increases the risk of suicide, just like firearms.

The CMI is legally required to provide information on side effects, special risks, overdose and storage. The TGA has allowed the CMIs to include no warning of the risk of these medications being used in a deliberate overdose. The TGA allows the CMIs to contain no advice on the safe storage of these medications to reduce the risk of deliberate overdose. The lack of information in the CMIs failed to provide people like myself with the ability to give informed consent to expose ourselves to this risk.

Studies show that specific medications that I have been prescribed are the amongst the most common medications causing death including:

- Valium
- Endone (Oxycodone)
- Mirtazapine
- Effexor XR
- Ciprimil (Citalopram)
- Panadeine Forte

The Coroners Court of Victoria in relation to the findings of the Inquest into the Death of David Andrew Trengrove stated that benzodiazepines are the most commonly found drug found in drug deaths. It also included information on drug groups that most frequently co-contributed with benzodiazepines in Victorian drug deaths in 2010. The groups listed include analgesics, antidepressants, antipsychotics and alcohol.

These medications are legally prescribed and PBS-funded, and the TGA has allowed the CMIs to contain almost no consumer warnings to help patients like me and their families protect against the use of these drugs in self-harm and suicides.

Suicide Attempts

In 2010-11 there were 20,499 hospitalisations in Australia due to intentional over-dose with medicines. One in three people admitted to hospital for intentional overdose had taken benzodiazepines or paracetamol, one in four had taken an antidepressant and one in six had taken an opioid medicine.[20]

Hospitalisation as a result of intentional over-dose

Table 1: Mechanism of intentional self-harm injury cases, Australia, 2010–2011[68]

Drugs, medicaments and biological agents	20,499
Psychotropic drugs	8,872 (43.3%)
Antidepressants	5,216 (25.4%)
Anti-epileptics, sedative-hypnotics, antiparkinsonism	8,523 (41.6%)
Benzodiazepines	7,158 (34.9%)
Non-opioid analgesics, antipyretics, anti-rheumatics	7,042 (34.4%)
Paracetamol	5,915 (28.9%)
Narcotics and psychodysleptics (hallucinogens)	3,764 (18.4%)
Other opioids	2,849 (13.9%)
Primarily systemic and haematological agents	1,243 (6.1%)
Drugs primarily affecting the cardiovascular system	783 (3.8%)
Drugs primarily affecting the autonomic nervous system	671 (3.3%)
Hormones and their synthetic substitutes and antagonists	612 (3%)
Systemic antibiotics	344 (1.7%)
Drugs primarily affecting the gastrointestinal system	292 (1.4%)
Other and unspecified drugs, medicaments and biological substances	1,034 (1.5%)

The medications I have been prescribed are not only toxic enough to be a means of death, statistics show it has been used for this purpose for decades, and still the TGA has taken no action to warn consumers. If this information has been made available to me, I would have ensured that I had safety measures in place that would have prevented my two medication overdoses.

More Information:

- PDLKZ: Chapters One, Two, Three, Four, Five, Six, Seven, Ten, Eleven, Twelve
- Patrick O'Connor, Professor Skerritt TGA Letter of Reply, 4th August 2020
- Patrick O'Connor, Professor Skerritt TGA Letter, 1st November 2020

13 Informed Consent

'Informed Consent' is the legal right of consumers to agree to medical treatment. It can only be given after being informed of all the benefits and risks of the treatment. So, if an adverse event happened, they had been made suitably aware it was a risk and willingly took that risk. The CMI is the source of information on medication endorsed by the Australian Department

[20] https://www.safetyandquality.gov.au/sites/default/files/migrated/Medication-Safety-in-Mental-Health-final-report-2017.pdf

of Health. It enables Australians to understand the side effects of a medication. This is a critical role in the informed consent process and millions of Australians, like me, rely on this information when taking a medication.

In Australia, the law relating to informed consent to treatment may be found in common law as well as legislation.

Australian law on disclosure of information about treatment predominantly stems from the High Court decision in Rogers v Whitaker. In that case, the Court stated that the term 'informed consent' 'is apt to mislead as it suggests a test of the validity of a patient's consent' (Mason CJ, Brennan, Dawson, Toohey, and McHugh JJ in Rogers v Whitaker 1992, at 490). Rather, it imposed a duty of care on medical practitioners to 'warn a patient of a material risk inherent in the proposed treatment' (at 490). Chief Justice Martin in Brightwater Care Group (Inc) v Rossiter (2009, para [30]) perhaps best summarised this Australian notion of 'informed consent' as 'a legal duty to inform patients of all aspects and risks associated with any medical procedure before seeking their consent to that procedure'. Chief Justice Martin stated that there was a similar obligation to provide patients with 'full information as to the consequences of any decision to discontinue treatment' (Brightwater Care Group (Inc) v Rossiter 2009, para [30]).[21]

13.1 Material Risks

'Informed consent' requires a consumer to be warned of all material risks prior to treatment. A risk is material if:

– a 'reasonable' person (in the same position) if warned of the risk is likely to attach significance to it, or

– if the medical practitioner is or should reasonably be aware that the particular patient, if warned of the risk, would be likely to attach significance to it.

Therefore, a known risk should always be disclosed to the patient when:

– an adverse outcome is common, even if the detriment is minimal

– an outcome is severe, even if its incidence is rare.

Given this, it is paramount that medical practitioners proposing medical treatments or procedures, inform their patients of the 'material risks' associated with the suggested treatment/procedure so they are able to make an informed decision about their healthcare.

This complaint focuses on life threatening side effects, with severe outcomes, that meet the definition of a material risk. These are the side effects and warnings that must legally be included in the CMI and are legally required to be disclosed to enable informed consent.

Informed consent can only be legally valid if it is informed. The TGA has the role of ensuring the CMI delivers this information to consumers. Yet the *Prescribed Deaths – Life in the Killing Zone* report details the systemic failings by the TGA in this role. In deciding to provide informed consent, a consumer is relying on a CMI that lacks all the material risks –

[21] Bernadette McSherry & Lisa Waddington (2017) Treat with care: the right to informed consent for medical treatment of persons with mental impairments in Australia, Australian Journal of Human Rights, 23:1, 109-129, DOI: 10.1080/1323238X.2017.1314808

so their consent is not informed. If the CMI does not replicate the description of risks provided by a doctor or pharmacist (and the TGA), then it has failed in its responsibility to support a patient making an informed decision. If the risks are not detailed, then they cannot be reinforced when a consumer reads the CMI at later times. The impact of the CMI not providing life-threatening side effect risks has significant legal implications.

The absence of many risks in the CMIs exist for individual drugs but most importantly, the gaps are bigger for polydrug treatments. Chapter 5 presents my position that if consumers have not had all the risks of these medications disclosed to them, then they did not receive all the information to provide 'informed consent'.

This is an issue that relates directly to my medication treatments. All of the prescribing doctors provided general information about the risks of the medications prescribed. However they all referred to the CMI for the comprehensive list of risks.

13.2 Ongoing informed consent to medication

Informed consent is not a one-time event. Each time the treatment is changed, it also changes the risk to the person, and those risks must be explained and informed consent given. Each time a medication is changed, a new medication is added, or a new dose prescribed, the associated risks have to be explained to the consumer and informed consent given. In the majority of my medication changes, my doctors referred me back to the CMIs to provide these risks. As all the material risks are not included in the CMIs, then the outcome was that my ability to provide 'Informed' consent at these later points of treatment with the medication was negatively impacted.

Confusion, memory difficulties and problems concentrating are acknowledged symptoms of depression and anxiety. In addition, many medications like benzodiazepines, have side effects that include drowsiness, dizziness, light headedness, confusion, memory problems and sedation. If the CMI does not replicate the description of risks provided by a doctor or pharmacist (and the TGA), then it has failed in its responsibility to support this advice when a consumer reads the CMI at later times. It impairs their ability to make an informed decision to take the medication.

On its own website, the TGA even states why the CMI is important, *They are a very useful back-up to help people remember the advice provided to them by their doctor.*[22] The Department of Health advises that "Keep all your CMIs in the one place so you can easily find them. You may also need to re-check some details while using the medicine." and "Always read the CMI before starting a new medicine. You may also want to refer to it while using the medicine — for example, to check if another medicine interacts with it, or what to do if you miss a dose." This would only be helpful if the CMI contained all the information that it is legally required to contain.

The law of informed consent requires consent to be given when new risks for a medication are known. When the TGA has either become aware of important side effects or was aware that new risks had been added to a CMI, it is their responsibility to ensure that existing users of the medication are provided with this Information. This is critical because in addition to being informed of the new risks, the consumer has to provide informed consent to continue to take the medication.

[22] https://www.tga.gov.au/blogs/tga-topics/not-so-much-tmi-cmi-empowering-consumers-clear-accessible-information-about-their-medicines

The report details the work of the TGA's opioid review, including the findings and the actions that are being taken. We included an analysis of the recent TGA review of the CMIs for opioid medications. Thankfully, warnings relating to coma, overdose, addiction, abuse, and death are finally being included. The warnings that the TGA requires the pharmaceutical companies to add are the same side effects that the report identifies as information that should have already been in the CMIs. It is not new information based on recent scientific developments, as evidenced by FDA opioid warnings dating back to 2001. The changes now being made to CMIs are an emphatic admission of the opioid risks that should have already been declared in the CMIs, and how consumers have been exposed to deadly risks for decades.

The new opioid CMIs detail a large number of changes to the CMIs that provide information that is the opposite to what was included in the previous CMIs. For example the new Endone 2020 CMI now states that *You can become addicted to ENDONE even if you take it exactly as prescribed.* Which is significantly different from the previous CMI which states *ENDONE can be addictive. If used for a long time ENDONE may become habit forming causing mental and physical dependence.* The new CMI also warns of the risk of death even when taking the medication as prescribed, a risk that has never previously been included in the CMI.

Simply updating a CMI or releasing a consumer update on the TGA website falls horrifically short of what is required to ensure our basic human right to safe healthcare is being upheld by the TGA. I have never been contacted by the TGA or a pharmacist on any new risks, warnings or CMIs. I have never been notified when filling a repeat prescription that a new CMI with new warnings is available.

The analysis of the CMIs shows that I have not been provided with all the life threatening side effects of individual medications and almost no information on the polydrug risks. The failure of the TGA to provide accurate and complete CMIs has directly impacted my legal right to provide informed consent since 2012 and continues to today.

More Information:

- PDLKZ: Chapters Four, Five, Six, Seven, Eleven
- Patrick O'Connor, Professor Skerritt TGA Letter of Reply, 4th August 2020

14 TGA Complaint

On the 7th July 2020, I emailed the report and a letter of complaint to Professor John Skerritt Deputy Secretary, Health Products Regulation Group Therapeutic Goods Administration. On the 23rd July I received a response from Professor Skerritt, which I replied to on the 4th August and as at the 25th November had not been responded to by Professor Skerritt. All letters are attached to this complaint.

Professor Skerritt did not address the findings for the individual medications analysed in the report or the breaches identified. His letter did not address the issues identified with the new CMIs and the failure of the TGA to ensure these new documents are provided to consumers. It is clear that he took deliberate steps to not comment on the specifics detailed in the report or my letter of complaint.

14.1 CMI vs PI

Professor Skerritt did comment broadly, on the issues relating to information being included in the PI but not in the CMI. In short he stated that not all information has to be replicated and that some information is too technical to be included in the CMI. He also suggests that referring a consumer to their doctor or pharmacist is sufficient in some instances. My response made these comments to those points:

CMI and PI risks

You state that the CMI and PI are not required to contain exactly the same content, which I agree would be impractical. The report doesn't suggest that the breaches relate to all the risks not being included in the CMIs. Rather, the side effects analysed are narrowed to those that pose a risk of adverse drug events or death. I am sure you would agree that this information is the content that must be included for medications with this level of danger, given that scheduled drugs are commonly found in drug death toxicology screenings.

In your reply you state that the CMI often describes more easily understood symptoms in lieu of the precise medical terminology. That is not a valid reason to exclude life-threatening side effects from CMIs, which is what the report shows has occurred at a systemic level for decades. In addition, I am confident that consumers (and carers) will be able to easily understand the meaning of side effects like addiction, dependence, abuse, respiratory depression, overdose, coma, and death. These are specific examples of the side effect descriptions used in PIs but withheld from CMIs. Poignantly, these are also the descriptions of the risks that the TGA is requiring pharmaceutical companies to belatedly add to opioid CMIs.

Professor Skerritt, you assert that some risks are actually not required to be included in the CMI, and that directing a person to a discussion with their doctor or pharmacist is sufficient. Your explanation is that the inclusion of this information in the CMI would require a high degree of medical literacy to understand. I am unable to identify any legislative provision that suggests this should be the case for disclosing life-threatening side effects. The CMI has a role to explain side effects and that is what it must do; consistent with the PI. Explaining and understanding life-threatening risks in the PI may require a high degree of medical literacy, but the law requires they be explained in an easy to understand way in the CMI. That is the purpose of the CMI. The CMI already includes general advice for consumers to seek further information if required from a doctor or pharmacist.

The Therapeutic Goods Regulations 1990 require information be provided to consumers on 'warnings and precautions, such as when the medicine should not be taken' ***and*** *warnings of the 'side effects' of taking a medication – these are separate requirements. Advising to not consume alcohol whilst taking the medication falls under 'warnings and precautions, such as when the medicine should not be taken.' Advising that the consumption of alcohol with the medication can result in respiratory depression, coma or death, is an explanation of potential 'side effects'.*

The CMI analysis in the report shows the failure to provide the information on the side effects and medication interaction that is legally required.

The reply from the department head of the TGA, in no way provided any information that refutes the detailed findings of the report. The analysis I have conducted focuses on side effects that meet the criteria of being *material risks*. I have also focused on risks that are described in the PI using easy to understand language, not medical terminology. The irrefutable evidence I have detailed is that life threatening risks explained in simple

language, exist in multiple PIs but have not been included in the CMI. These are clear breaches of the *Therapeutic Goods Act 1989,* and what is even clearer is the failure of the TGA to take any action on this matter. In our research, we have been unable to identify a single instance of when the TGA has taken action for a single breach of this nature.

14.2 TGA Failings

My reply to Professor Skerritt on the 4th August also detailed multiple examples of when the TGA has failed to ensure life threatening risks have been included in CMIs and still is. This can be found in that letter under the headings:

- TGA consumer warnings
- TGA industry briefing
- New Opioid CMIs
- Panadeine Forte
- Consumer updates
- Nyxoid
- Self-harm and suicide
- Valium
- Alprazolam
- TGA and FDA
- New CMIs
- TGA and FDA
- Opioid Crisis
- Human Rights

More detail on other TGA failings can be found in Chapters Two, Three, Four, Five, Six, Seven, Nine, Elven, Thirteen

New CMIs

The TGA is introducing a new format that will be implemented for all medicines that require a CMI. The format is important, but it is the content of the CMI that is critical. The template for the new CMI provides specific sections that provide for specific risks to be detailed[23]. For example:

Some medicines may interfere with [medicine name] and affect how it works.
[Include an explanation of the nature of the interaction where possible] e.g.

Drinking alcohol
Tell your doctor if you drink alcohol.
Alcohol may [insert effect relevant to use of the medicine].

Less serious side effects

Less serious side effects	***What to do***
[Grouping 1 as per effect on body e.g. bleeding-related]: *[list as appropriate]* ***[Grouping 2 as per effect on body]:***	***Speak to your doctor if you have any of these less serious side effects and they worry you.*** ***[Insert appropriate action]***

[23] https://www.tga.gov.au/improved-consumer-medicine-information-template

[list as appropriate]	

Serious side effects

Serious side effects	***What to do***
[Grouping 1 as per effect on body e.g. bleeding-related]: *[list as appropriate]* ***[Grouping 2 as per effect on body]:*** *[list as appropriate]*	***Call your doctor straight away, or go straight to the Emergency Department at your nearest hospital if you notice any of these serious side effects.***

The new opioid CMIs now contain warnings that combining them with other medications like benzodiazepines, other pain relievers, antidepressants, and antipsychotics, may result in severe drowsiness, decreased awareness, breathing problems, coma and death. There is no information on what changes will be made to the risks included in the new non-opioid CMIs and if risks like these will be added.

The TGA website contains information on the new template. The webpage titled *Using the TGA CMI template: Guidance for sponsors* reinforces the legal requirements of a CMI:

The updated regulations maintain the previously established general requirements that CMI documents must be:

- *written in English*
- *clearly legible*
- *written in language that will be easily understood by consumers*
- *consistent with Product Information about the product.*

The new Panadeine Forte and Endone CMIs are analysed in the 4th August reply to Professor Skerrit. The analysis shows that even after the TGA review of the CMIs, and the addition of some new warnings, the systemic practice of withholding material risks from consumers continues. The clear legal requirement that the CMI is consistent with the PI has not changed. Despite this it is clear that pharmaceutical companies are still exploiting the failure of the TGA to regulate the contents of the CMI to ensure it is consistent with the PI. It is also clear that the TGA has no intention of taking action to correct this.

Panadeine Forte

The Panadeine Forte CMI was updated in May 2020[24] by Sanofi-Aventis. Many risks have been added to the CMI as part of the TGA's review. Incredulously, many life-threatening risks have still been withheld from the CMI, and yet these risks are detailed in the Panadeine Forte May 2020 PI[25] that the TGA has approved for healthcare professionals. At a glance:

1. *Addiction*: The PI states that the risk of addiction is increased in patients with a personal or family history of substance abuse (including alcohol and prescription and illicit drugs) or mental illness. The comorbidity of mental illness and pain conditions is well known, so how can this warning not be included and highlighted in all opioid CMIs?

[24] Sanofi Aventis Panadeine Forte May 2020 CMI
[25] Sanofi Aventis Panadeine Forte May 2020 PI

2. *Addiction*: The PI states that the risk also increases the longer the drug is used and with higher doses.
3. *Alcohol*: The PI warns of the risk of respiratory depression, coma and death when consuming alcohol.
4. *Overdose*: The PI warns of the risk of respiratory depression, coma, cardiac arrest and death if an overdose occurs, especially by children. The CMI does state that an overdose can occur at prescribed levels, making the need to explain the dangers of an overdose even more critical.
5. *CYP 2D6 gene*: The PI warns of the fatal risks of this medication to children who have the CYP 2D6 gene.
6. *Children*: The PI warns of the risk of death to children post tonsillectomy and/or adenoidectomy.
7. *Tolerance and Dependence*: The PI states the development of tolerance and physical dependence and risks of adverse effects, including hazardous and harmful use, that increases with the length of time a patient takes an opioid.
8. *Pregnancy*: The PI states that it may cause respiratory depression and withdrawal syndrome in neonates and newborn infants.
9. *Breastfeeding*: The PI warns of the risk of respiratory depression, morphine overdose and opioid toxicity and death for newborn infants.
10. *Opioid*: The PI states this medication is an opioid.

These risks are not included in the CMI and are clear instances of when the CMI is not consistent with the PI.

Subsequent to the report's release, we have further analysed the new Endone April 2020 CMI with the Endone April 2020 PI[26] to identify further inconsistencies. Risks 1, 2, 3, 4, 8 and 10 as detailed for Panadeine Forte above, also apply to the Endone PI. Likewise, these risks are not included in the Endone April 2020 CMI, detailing areas in which the CMI is again not consistent with the PI.

More Information:

- Patrick O'Connor, Professor Skerritt TGA Letter of Reply, 4th August 2020

15 Failure of pharmacists to provide medication warnings

This second part of this complaint focuses on the provision of advice and consumer warning information in my interactions with pharmacists since 2012. In the majority of the times when pharmacists have dispensed my medication I have not been offered advice or a CMI. In some instances advice has been provided that is inaccurate and increased the risk of side effects occurring.

The *National Health Act 1953* regulates the provision of medicines, and agreements with pharmacists also stipulate the legal requirements for consumer medication safety. The failure of pharmacists to uphold these requirements in the provision of medication warnings to me is a breach of ethical and legal requirements.

[26] Aspen Endone April 2020 PI

Chapter Four of the report details the role of pharmacists in the delivery of PBS medication and safety standards.

The *National Health Act 1953* [27] details the role of the Australian Government in providing pharmaceutical medications to Australians. Since 1990 the programs, services and remuneration that pharmacists receive for dispensing PBS medicines has been governed by a series of agreements. The latest agreement is the Seventh Community Pharmacy Agreement[28]. Part 1 of this Agreement is between the Commonwealth and the Pharmacy Guild of Australia and includes an agreement for the purposes of section 98BAA(1) of the National Health Act 1953 (Cth). Part 3 of this agreement is between the Commonwealth, the Guild and the PSA.

15.1 The Seventh Community Pharmacy Agreement

The Seventh Community Pharmacy Agreement (7CPA) commenced 1 July 2020.

The 7CPA is an agreement between:

- the Commonwealth Government
- the Pharmacy Guild of Australia
- the Pharmaceutical Society of Australia (PSA)

The 7CPA will be in place for five years until 30 June 2025.

This agreement not only outlines the provision of medication, but also the provision of the CMI for each medication and verbal advice provided to consumers. Payment for the provision of CMIs by pharmacists was specified as part of the dispensing fee in the Fourth Community Pharmacy Agreement of 2005.

Section 7 of the 7CPA places a clear obligation on the pharmacy owner (Approved Supplier) to ensure that all legal and professional requirements are met, otherwise they could be guilty of defrauding the Government.

7.1 The Guild and its members recognise that, by submitting a PBS or RPBS claim, Approved Suppliers are acknowledging that they have complied with all relevant Commonwealth, State and Territory legislative requirements for the dispensing of a PBS or RPBS medicine, including:

> *7.1.1 the codes, guidelines and policies established by the Pharmacy Board of Australia (or any other registering authority);*
>
> *7.1.2 the codes, guidelines, professional practice standards and competency standards established by the PSA;*
>
> *7.1.3 the standards and requirements as established by other authorities, including the Therapeutic Goods Administration and Society of Hospital Pharmacists of Australia (as applicable to specialised areas of practice);*
>
> *7.1.4 any regulations or requirements as established by States and Territories with respect to one or more of the registration, practice or handling of medicines established within that State or Territory;*

[27] https://www.legislation.gov.au/Details/C2020C00228
[28] https://www1.health.gov.au/internet/main/publishing.nsf/Content/New-7th-Community-Pharmacy-Agreement

7.1.5 all applicable State, Territory and Commonwealth laws with respect to the conduct of their profession; and

7.1.6 any other requirements not stated above but that are covered by the National Health (Pharmaceutical Benefits) (Conditions of approval for approved pharmacists) Determination 2017.

Section 15 of the 7CPA details the provision of CMI.

15.1 Consumer medicines information (CMI):

15.1.1 is free, reader-friendly documentation that provides information about prescription medicines;

15.1.2 answers common questions about the medicine; and

15.1.3 is a valuable resource for patients and should be provided in conjunction with counselling from a health professional.

15.2 Recognising the benefits of CMI, the Guild will ensure that Approved Pharmacists provide CMI to patients in accordance with all relevant professional practice standards and guidelines, including Standard 6 (Medicines Information) of the PSA's Professional Practice Standards, as clinically appropriate.

15.2 The PSA Professional Practice Standards

The PSA's Professional Practice Standards (PPS) articulate the expected standards of professional behaviour of pharmacists in Australia. Pharmacists have an ethical and legal commitment to the community to ensure safe and effective delivery of pharmacy services; the PPS enable the profession to qualitatively and quantitatively measure the commitment to the quality and reliability of healthcare services and products.

Standard 6: Medicines Information[29]

6.4 Ensuring that information is accurate, relevant, timely and understood.

This means that the information provided by pharmacists including verbal advice and printed advice like the CMI, is accurate content, including the risks and warnings of taking the medication. It also requires the pharmacist to ensure the information is understood.

6.4 Providing adequate and balanced information to enable individuals to make informed medication and healthcare choices.

This reinforces the importance of the information provided to the legal right of informed consent.

6.4.6 Applies evidence-based practice principles to provide accurate, timely and tailored medicines and health information to patients, authorised representatives and communities.

The importance of tailored medicines information is critical to many patients with disabilities. The use of multiple medications increases the risk of adverse side effects. The information given must be specific to the polydrug combinations as they relate to that individual.

[29] Professional Practice Standards – Version 5 – June 2017 Edition: 5th Pharmaceutical Society of Australia

In addition, *Standard 16: Harm Minimisation*, provides further requirements in the handling of medication safety warnings to consumers.

Section 16.7 requires *Collecting or obtaining access to minimum essential information, including current prescription and non-prescription therapies, health conditions, allergies, adverse effect and patient preferences.*

16.7.2 Collects or accurately records sufficient patient details, and a complete medication and health history in the healthcare record to optimise harm minimisation services.

16.7.6 Synthesises all available information with informed professional judgement to formulate and present the most appropriate counselling, lifestyle advice and treatment options to the patient.

16.7.7 Confirms that all health and medicines information, and healthcare plans are current and accurate.

16.7.8 Gathers information and records details of any adverse drug reactions, including allergies, precautions and contraindications known to the patient.

16.7.9 Accesses current information on clinically significant interactions, contraindications, precautions and disease states.

16.7 Assessment, consultation and reconciliation • Ensuring a thorough, accurate and systematic approach to history taking. • Identifying the most appropriate time(s) in the counselling process to take a history or repeat history taking. • Documenting essential information. • Collecting or obtaining access to minimum essential information, including current prescription and non-prescription therapies, health conditions, allergies, adverse effects and patient preferences.	Meets actions outlined in *Standard 3: Dispensing and Other Supply Arrangements, Criterion 3.5: History taking*, and *Criterion 3.6: Assessment, consultation and reconciliation.*
	16.7.1 Establishes a patient healthcare record (profile).
	16.7.2 Collects or accurately records sufficient patient details, and a complete medication and health history in the healthcare record to optimise harm minimisation services.
	16.7.3 Documents any special needs of the patient in their profile so that counselling and associated resources can be tailored accordingly.
	16.7.4 Assesses factors likely to influence the reliability of sources (e.g. the patient as a historian).
	16.7.5 Checks the dispensing history and/or electronic healthcare record to determine the appropriateness of information being sought and provided.
	16.7.6 Synthesises all available information with informed professional judgement to formulate and present the most appropriate counselling, lifestyle advice and treatment options to the patient.
	16.7.7 Confirms that all health and medicines information, and healthcare plans are current and accurate.
	16.7.8 Gathers information and records details of any adverse drug reactions, including allergies, precautions and contraindications known to the patient.
	16.7.9 Accesses current information on clinically significant interactions, contraindications, precautions and disease states.

These requirements of the standard provide a very clear and defined service that is required by pharmacists. They must keep an accurate list of all the patients medications, and any specific medication problems, which will facilitate tailored information to the patient.

15.3 PSA Code of Ethics and Dispensing Practice Guidelines

Chapter Four of the report details the other relevant professional practice standards and guidelines that relate to the provision of a CMI, including the PSA *Code of Ethics* and *Dispensing Practice Guidelines*. The dispensing guidelines outlines when patient counselling is required and that a CMI is an important part of that process. The *Dispensing Practice Guidelines* states that *Pharmacists also have a professional obligation to provide all necessary and up-to date information to enable patients to make informed decisions about their medicines. CMI leaflets should be regarded as a valuable tool for assisting the counselling process, not as an alternative to counselling.*

The Guideline also states that *Information contained in CMI leaflets is brand specific and must be consistent with the approved Product Information (PI).* In the section titled *Providing CMI Leaflets* the guidelines state that, *Patients should have the opportunity to access the current version of the CMI leaflet each time a product is dispensed.*

The Guideline outlines the following circumstances that are appropriate for patient counselling;

– the patient is new to the pharmacy

– the medicine is new for the patient or there is a change in strength from a previous prescription

– there are special administration instructions for the medicine

– the prescription is for a child, an older person, or a person at risk of medication misadventure (e.g. polypharmacy)

– there are special patient needs (e.g. visual, auditory or cognitive impairment; cultural and linguistic diversity)

– the medicine has a narrow therapeutic index or requires therapeutic monitoring

– the medicine is a controlled drug.

– after each supply of medicine

– regular reinforcement of information may be required (e.g. if the medication is cytotoxic or teratogenic, or has major contraindications for its use)

– at regular intervals for medicines used for long-term therapy (e.g. every 6 months, or on dispensing the last repeat of a prescription with five repeats)

– when the pharmacist has received advice that a sponsor has made significant changes to the CMI.

Based on these guidelines, the medications I have been prescribed and the length of my treatment, I should have been offered counselling and a CMI on almost every pharmacy visit. I can reliably state that I have been offered a CMI or counselling in less than 10 of the 200 pharmacy visits since 2012. All of these instances was when a medication was being dispensed for the first time. I can also reliably state that I have never been offered a CMI when I was new to pharmacy, there was a change in strength, polypharmacy, due to my cognitive impairment, narrow therapeutic index (e.g. Lithium Carbonate), controlled drug

(e.g. Dexamphetamine), each supply, major contraindications (e.g. Endone), regular intervals or due to a sponsor making changes to a CMI.

This has also not occurred in the visits to pharmacies since July 2020, which is the commencement of the 7CPA.

I have also never been advised by a pharmacist that the information in the CMI lacks side effects and warnings that are present in the PI. The pharmacist is also responsible for ensuring ensuring that the information I receive is up to date and accurate, a responsibility they have clearly failed to deliver to me.

These guidelines are also replicated in the Pharmacy Board of Australia, *Guidelines for dispensing of medicines*[30]*. The guideline provides guidance to those registered in the profession in relation to a matter of professional practice, not set down in the legislation or a registration standard, which can be used in proceedings under the National Law as evidence of what constitutes professional conduct or practice for the health profession.*

15.4 Community Pharmacy Service Charter

The PSA code of ethics is also supplemented with the Community Pharmacy Service Charter. The charter covers a number of key areas to ensure consumers are provided with safe and effective healthcare. This charter also covers some of the services that pharmacists are paid fees by the PBS for.

Community Pharmacy Service Charter

We will provide medicines and pharmacy related services and products to address your healthcare needs. We will provide safe and effective medicines and high quality pharmacy related services, with professional care, skill and competence.

We will answer questions about medicines, as well as give useful information about health conditions.

Safety

Our pharmacy ensures that our staff are qualified and trained, and comply with professional standards, guidelines and codes of conduct.

Communication

I have a right to be informed about services, treatment, options and costs in a clear and open way.

We will provide you open, timely and appropriate communication about your health, medicines and related services in a way you can understand.

Participation

I have a right to be included in decisions and choices about my care.

We will include you in making decisions and choices about your health, medicines and related services and products.

[30] https://www.pharmacyboard.gov.au/documents/default.aspx?record=WD15%2f17695&dbid=AP&chksum=cZm3mO8R6fTMdPPl3scPUw%3d%3d

15.5 Pharmacy Advice

My complaint against pharmacists is not only about the failure to provide the CMI, but also the verbal information that has been provided when I have sought advice. Chapter Four contains details of my personal experiences of pharmacy visits for advice on Endone and Valium, 2 medications that I have been prescribed. The process involved asking for warning information about the side effects of prescription opioids (Endone) and benzodiazepines (Valium). The questions focused on the polydrug interactions, and what the worst side effects could be. The risk of taking alcohol was also raised given it is a lethal polydrug combination. Combining these classes of drugs is deadly and are the leading cause of drug deaths in Australia.

Subsequent to the release of the report, to further highlight the lack of commitment to medication safety by ACT pharmacists, I undertook further visits to an additional 5 pharmacists on the 7th July in the ACT and record the conversations. The purpose of the visit was to ask for the most recent warning document for Panadeine Forte that I am prescribed, which is the Sanofi-Aventis Panadeine Forte May 2020 CMI. I also asked if having a mental illness increases the risk of addiction to the medication (a known risk detailed in the May 2020 PI).

Four of the five pharmacists provided the Panadeine Forte CMI from 2017, and all were asked and confirmed it was the most recent CMI available. Of these four pharmacies, three advised that there was no greater risk of addiction for a person with a mental illness and one was unsure. A fifth pharmacist advised that the medication was not addictive to anyone, that it was safe if taken as directed and that no consumer warning document has ever been produced for the medication. As an individual currently prescribed this medication, these 3 statements placed me in an increased level of medication danger and death.

In all visits I have documented, none of the pharmacists verbally provided the life-threatening warnings as well as the hard copy CMIs. Every single visit failed to advise of the information (as outlined by the Department of Health and the TGA) in relation to the life-threatening risks these medications expose a person to. Multiple times, information was given verbally that is factually incorrect and misleading as to the life-threatening risks. These visits where undertaken to provide recorded evidence to confirm the position of people with lived experience like me, that pharmacists are failing to provide the critical information on the side effects of medication.

15.6 Pharmacist Failures

Pharmacists have a critical role in medication safety, a role they are remunerated for and which is regulated by numerous ethical and legal standards. Despite this complaints against pharmacists by people with lived experience for their failure to meet these standards has been consistent for decades. The Department of Health has ignored these complaints. It defies any form of logic, that the profession responsible for dispensing the CMI has failed to identify and address the warnings that are not present in these documents. Pharmacists have access to the PI for each medication and sophisticated drug warning software. It is a horrific failure that the profession responsible for dispensing CMIs, has failed to check they contain the side effects that they are legally required to contain.

The Pharmacy Guild has publicly stated that they are committed to the provision of the CMI

One such approach is the commitment that the Guild will ensure that community pharmacists provide Consumer Medicines Information to patients. The Agreement

recognises the CMI must be free, reader-friendly documentation that provides information about prescription medicines and answers common questions about the medicine. It reinforces that the CMI "is a valuable resource for patients and should be provided in conjunction with counselling from a health professional". Again, the patient is the focus.[31]

Unfortunately my personal experience demonstrates that this is a commitment that has not transferred into any action.

More Information:

- PDLKZ: Chapters Four, Five, Six, Seven
- Patrick O'Connor, Professor Skerritt TGA Letter of Reply, 4th August 2020

16 Convention on the Rights of Persons with Disabilities

My complaint presents the personal experiences that detail how I have not been provided with the legally required side effects of medication I have been prescribed. These issues are summarised as follows:

- Failure of the TGA to ensure the CMI is legally compliant
- Failure of the TGA to advise when additional risks had been added to a CMI
- Failure of pharmacists to provide the CMI
- Failure of pharmacists to provide accurate advice

The laws that I argue have been broken include:

- *Therapeutic Goods Act 1989*
- *National Health Act 1953*

I believe that these legal failures have breached multiple articles of the CRPD. This includes rights to information, legal capacity, informed consent, abuse and good health.

Chapter Five of the report includes analysis of the UN Convention on the Rights of Persons with Disabilities. The Convention identifies general and specific obligations on States parties in relation to the rights of persons with disabilities. In terms of general obligations, States have to:

- protect and promote the rights of persons with disabilities in all policies and programmes;

- stop any practice that breaches the rights of persons with disabilities;

- ensure that the public sector respects the rights of persons with disabilities;

- ensure that the private sector and individuals respect the rights of persons with disabilities;

Countries that join in the Convention engage themselves to develop and carry out policies, laws and administrative measures for securing the rights recognized in the Convention and abolish laws, regulations, customs and practices that constitute discrimination (Article 4).

[31] https://www.guild.org.au/news-events/news/forefront/v10n13/patient-outcomes-focus-of-7cpa

This complaint against the Australian Government alleges that by failing to ensure that medication safety standards have been maintained through the *Therapeutic Goods Act 1989* and the *National Health Act 1953,* that my human rights under the CRPD have been breached.

By failing to ensure that CMIs contain all the legally required risks and warnings of my medications, the government has exposed me to side effects that I was deliberately left unaware of.

The failure to provide this information has also left me unable to provide legally valid informed consent to the medication treatment.

The failure of the government to ensure that I have been provided CMIs through dispensing pharmacists, has also exposed me to side effects and impacted my ability to provide informed consent.

The verbal advice provide by pharmacists, has also failed to provide me with the side effects and warnings of the medications prescribed.

This complaint also details how the TGA and Department of Health have failed to act on these issues, despite being aware of them for over ten years.

The cognitive impairment due to my conditions and the cognitive impairment due to the side effects of the medications prescribed, have not been recognised in the process of delivering information to myself. The process of communicating the information completely fails to provide the critical warnings in a manner that accommodates the mental state of patients.

The articles of the CRPD that I understand are applicable to this complaint include[32]:

Article 25: Health

People with disability have the right to the enjoyment of the highest attainable standard of health without discrimination.

d) Require health professionals to provide care of the same quality to persons with disabilities as to others, including on the basis of free and informed consent by, inter alia, raising awareness of the human rights, dignity, autonomy and needs of persons with disabilities through training and the promulgation of ethical standards for public and private health care;

Article 21 – Freedom of expression and opinion, and access to information

States Parties shall take all appropriate measures to ensure that persons with disabilities can exercise the right to freedom of expression and opinion, including the freedom to seek, receive and impart information and ideas on an equal basis with others and through all forms of communication of their choice, as defined in article 2 of the present Convention.

(a) Providing information intended for the general public to persons with disabilities in accessible formats and technologies appropriate to different kinds of disabilities in a timely manner and without additional cost;

[32] https://www.ohchr.org/EN/HRBodies/CRPD/Pages/ConventionRightsPersonsWithDisabilities.aspx

Article 9 – Accessibility

To enable persons with disabilities to live independently and participate fully in all aspects of life, States Parties shall take appropriate measures to ensure to persons with disabilities access, on an equal basis with others, to the physical environment, to transportation, to information and communications, including information and communications technologies and systems, and to other facilities and services open or provided to the public, both in urban and in rural areas.

(b) Information, communications and other services, including electronic services and emergency services.

Article 10 – Right to life

States Parties reaffirm that every human being has the inherent right to life and shall take all necessary measures to ensure its effective enjoyment by persons with disabilities on an equal basis with others.

Article 12 – Equal recognition before the law

1. States Parties reaffirm that persons with disabilities have the right to recognition everywhere as persons before the law.

2. States Parties shall recognize that persons with disabilities enjoy legal capacity on an equal basis with others in all aspects of life.

3. States Parties shall take appropriate measures to provide access by persons with disabilities to the support they may require in exercising their legal capacity.

4. States Parties shall ensure that all measures that relate to the exercise of legal capacity provide for appropriate and effective safeguards to prevent abuse in accordance with international human rights law.

Article 16 - Freedom from exploitation, violence and abuse

1. States Parties shall take all appropriate legislative, administrative, social, educational and other measures to protect persons with disabilities, both within and outside the home, from all forms of exploitation, violence and abuse, including their gender-based aspects.

17 Required Complaint Resolution

The outcome I am seeking can be summarised into 4 areas:

- Urgent action is required to update all relevant CMIs and to ensure all existing users of these medications are made aware of the risks not previously disclosed
- The TGA to commence approving all CMIs before they are made available to consumers
- Acknowledgement of the retrospective breaches and action taken against the companies responsible
- Pharmacists are policed to ensure they deliver their obligations to provide advice and the CMI to consumers

Opioids, benzodiazepines, codeine, antidepressants, antipsychotics, mood stabilisers and amphetamines are medications that have been prescribed to me since 2012. The risks that have not been included in the CMIs are risks that I have been exposed to, risks that have impacted my health and nearly cost me my life on two occasions. This complaint is not only about systemic issues that exist with medication safety, it is also a complaint to the TGA about my personal adverse drug experiences with these medications. The specific action that I am seeking is detailed in section 4.2 on page 349 of the report, however I am prepared to discuss this further, with a view to achieving a fast outcome to save the lives of vulnerable Australians.

18 Additional References

18.1 Patrick O'Connor, TGA Letter of Complaint, 7th July 2020

18.2 Professor Skerritt, Patrick O'Connor Letter of Reply 23rd July 2020

18.3 Patrick O'Connor, Professor Skerritt TGA Letter of Reply, 4th August 2020

18.4 Patrick O'Connor, Professor Skerritt TGA Letter, 1st November 2020

Adjunct Professor John Skerritt
Deputy Secretary, Health Products Regulation Group
Therapeutic Goods Administration
PO Box 100
Woden ACT 2606

Dear Professor Skerritt

The purpose of this communication is to lodge a formal complaint against the Therapeutic Goods Administration (TGA) for failing to maintain medication safety regulations under the *Therapeutic Goods Act 1989.*

The attached report, *Prescribed Deaths – Life in The Killing Zone*, documents the areas in which the TGA has failed to meet medication safety standards for all Australians. The most vulnerable members of our society, including people with disability, the elderly, children, Indigenous Australians, first responders and veterans, are the most severely affected.

This report has undertaken a detailed assessment of 10 medications prescribed in Australia through the Pharmaceutical Benefits Scheme (PBS). The analysis shows that pharmaceutical companies have been producing consumer medication information (CMI) documents that **deliberately include misleading, inaccurate and incomplete information on the life-threatening risks of taking these medications for more than 20 years**. These risks include addiction, overdose, coma and death. For the 10 medications analysed, we identified 46 instances where the warnings represent breaches of the *Therapeutic Goods Act 1989*. The medications are:

1. Oxycontin
2. Endone
3. Valium
4. Xanax
5. Efexor
6. Lithium
7. Durogesic
8. Fluoxetine
9. Targin
10. Dexamphetamine.

The core function of the CMI is to provide information on the risks of a medication to consumers and this information is used in their decision to give informed consent. The CMI is presented as the reliable source of truth for consumers; it is the document that consumers are directed to for medication information by the healthcare system and government.

This report shows that the **exact risks not disclosed are directly or indirectly linked to the majority of Australia's adverse drug events and deaths**. The cause and effect cannot be any clearer and the people affected are vulnerable people who are prescribed these medications.

Human Rights

The rights of vulnerable people – in fact, all people – to safe healthcare is enshrined in the Universal Declaration of Human Rights, the Australian Charter of Healthcare Rights, and the Convention on the Rights of Persons with Disabilities. It is a legal requirement that medical treatment, including taking medication, can only commence after we give our informed consent. For the consent to be valid, it has to be informed, meaning that we have been provided with all the information about potential risks of taking the medication. This includes when multiple medications are prescribed.

The law provides us with the right to full disclosure of all risks – there is no discretion, even for risks that might be deemed rare in occurrence. Our CMI analysis is emphatic in demonstrating dangerous risks have not been disclosed for the most commonly prescribed medications for people with mental illness and pain conditions. Millions of people have given consent, without being informed, and hence their consent is not legally valid. You simply cannot assess a risk that you don't know about. You cannot follow safety advice if it has never been given to you. The resulting impact on human life has been physical illness, dangerous side effects and for many, death.

CMI Updates

This report includes analysis of the recent TGA review of the CMIs for opioid medications. Thankfully, warnings relating to coma, overdose, addiction, abuse and death are finally being included. The TGA states that the "improvements to information for prescribers and patients [are to] encourage best-practice prescribing and help consumers to be better informed about the potential risks and how to mitigate them".

Consumers can only give informed consent to taking medication if they have been fully informed. The changes now being made by the TGA are an emphatic admission of the opioid risks that consumers have not been provided within the CMIs for decades. These risks have been well-documented in manufacturer and government literature for many years. The only group who will be seeing this information for the first time will be consumers. However, they will only see these new warnings *if they ask for them*.

The pharmacists we spoke to in the preparation of this report were unaware of the recently updated CMIs, and therefore, the critical warnings remain unknown to those filling or re-filling their prescriptions. More disturbingly, there is no legal requirement for them to do so anyway, nor is there any direction from the TGA to inform consumers currently being prescribed these medications.

It is important to state again that being informed of all risks is a legal right. When new risks are presented to a consumer it necessitates that individual to be asked to give informed consent to these new risks. Simply updating a CMI falls horrifically short of what is required to ensure basic human rights to safe healthcare being upheld by the TGA.

Still Failing to Warn Consumers

In addition to the 10 medications examined in Chapter 2 of the report, we also analyse the commonly prescribed medication, Panadeine Forte. The June 2017 CMI does not contain a single mention of the risk of death, addiction, dependence, tolerance, withdrawal or abuse. It contains no mention of the lethal side effects of using this medication with alcohol or benzodiazepines. In total, we identified 14 areas as breaches of the *Therapeutic Goods Act 1989*. This medication has been in use for 20 years and is attributed as the cause of death for hundreds of Australians in many government studies.

The Panadeine Forte CMI was updated in May 2020 by Sanofi-Aventis. For the first time, it now includes warnings of the risk of death, addiction, dependence, tolerance, withdrawal and abuse. It also now includes the risk of death when using the medication with a benzodiazepine, a common cause of drug death in Australia over the last 20 years. Incredulously, many life-threatening risks have still been overlooked, and yet these risks are detailed in the May 2020 Panadeine Forte Product Information (PI) that the TGA has approved for healthcare professionals. Why has the TGA not ensured these risks are included in the May 2020 Panadeine Forte CMI?

For example, the PI states that "The risk of addiction is increased in patients with a personal or family history of substance abuse (including alcohol and prescription and illicit drugs) or **mental illness**". The comorbidity of mental illness and pain conditions is well known, so how can this warning not be included and highlighted in all opioid CMIs?

The CMI still fails to warn of the risk of death when consuming alcohol or if an overdose occurs. The CMI does state that an overdose can occur at prescribed levels, making the need to explain the dangers of an overdose even more critical. The fatal risks of this medication to children who have the CYP 2D6 gene is still inadequate, and it is unclear why the CMI still does not describe the medication as an opioid. The absence of life-threatening neonatal risks in the PI is incredibly disturbing.

While the TGA has improved the level of information in the opioid CMIs, unfortunately there are still significant gaps in the material risks disclosed in comparison to the PIs. It is simply unconscionable that these risks are excluded from the CMIs, as is the fact that the polydrug risks have not been added to other CMIs like benzodiazepines, antipsychotics and antidepressants.

Urgent Action is Required

This report has documented multiple medication safety failures, across multiple classes of medication. This report also proposes a number of recommendations to immediately stop the adverse prescription drug events and deaths being suffered by too many Australians.

The urgency of this matter cannot be understated. The current global health crisis has seen an increase in the number of Australians seeking help for mental health conditions. The issues examined in this report demonstrate that Australians will continue to be exposed to further adverse health events caused by systemic failures to provide safe healthcare if action is not taken.

Regards

Patrick O'Connor
[redacted]

07 July 2020

Australian Government
Department of Health

Deputy Secretary

Mr Patrick O'Connor
[redacted]

Dear Mr O'Connor

Your letter and report, 'Prescribed Deaths – Life in the Killing Zone'

Thank you for your correspondence dated 7 July 2020 and the attached report. I note the significant investment of time and effort that has gone into writing the report.

I am responding on the regulatory issues you have raised relevant to the Therapeutic Goods Administration (TGA), which is part of the Department of Health. Although I acknowledge that you have also raised important and related clinical practice matters such as informed consent, the regulation of the health profession is the responsibility of the Medical Board of Australia.

In your letter and report, you express specific concerns about the content of Consumer Medicines Information (CMI) documents for a number of medicines, relative to the content of their corresponding Australian Product Information (PI).

Pharmaceutical companies have the responsibility to write and maintain their CMI; TGA does not have a role approving CMIs. As you identify in your report, the CMI is required by the *Therapeutic Goods Regulations 1990* to be consistent with the PI. However, I should clarify that they are not required to contain exactly the same content. This is chiefly because, although both are publically available, the information contained in the PI is targeted at health professionals whereas the CMI is predominantly for patients and their carers.

The Regulations also require that the CMI is written in language that will be easily understood by patients and therefore the content is often less technical than that found in the PI. For example, a CMI often describes more easily understood symptoms in lieu of the precise medical terminology for individual side effects. Similarly, it usually advises the importance of having further discussions with the prescribing doctor or the dispensing pharmacist, particularly if the consumer has any concerns or questions about using the medicine.

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For example, in a situation such as you have described on page 109 of your report, where there is a specific neonatal or foetal risk included in the PI, it would be considered consistent for the CMI to instead advise the patient to speak with their doctor if they are pregnant, planning to become pregnant or breastfeeding. This is because the inclusion of additional technical details would require a high degree of medical literacy (which sadly is comparatively low in Australia) and could have the potential to confuse and delay action by patients.

While PI and CMI are important tools to assist prescribers and consumers to be aware of potential risks, they are not intended to be a substitute for individualised health professional advice or informed consent, which are clinical practice matters. Prescribing decisions may also be informed by clinical guidelines and other resources published by clinical colleges.

You may be aware that the TGA has recently undertaken a project to further reduce complexity and improve readability of CMIs. This has resulted in the development of a new format that based on extensive consumer testing provides more accessible safety and other information for consumers. This new format will be implemented for all new medicines that require a CMI from the start of next year and adopted other medicines within a set transition period. Pharmaceutical companies can elect to adopt the new format sooner and some have already indicated their intention to do so.

While our regulatory remit is limited to medicines and other therapeutic goods, the TGA does work to improve awareness of potential safety issues to influence prescriber behaviour. For example, the opioid reforms that you have mentioned have the overall aim to reduce harmful and hazardous use of these products while maintaining appropriate use. This is resulting in stronger warnings in the PI and CMI of these products in addition to a number of other changes that have been informed by an advisory group of clinical experts and consumer representatives.

We are undertaking a range of other activities in conjunction with various clinical groups to support the opioid reforms and provide health professionals with the tools and resources to apply them in practice. There will also be a range of resources for consumers to empower them to make informed choices about their treatment.

While responding to opioid issues is currently a priority, the TGA also continues to monitor and respond to issues concerning other medicine classes, including antidepressants, benzodiazepines and gabapentinoids.

Your letter directed us to the recommendations made in your report. I am unable to comment on many of the recommendations that require specific Government action like a Royal Commission, or a new healthcare safety regulator, as a decision on these would be for the Parliament to make.

In relation to your recommendations in section 4.2 of the last chapter of your report, the TGA applies scientific and clinical expertise to decision-making to ensure that the benefits of a medicine outweigh its risks across the lifecycle of a medicine for its intended population. While there may be variation in some processes, TGA standards are aligned with those employed by other medicines regulators including

the FDA and the EMA, and we collaborate and communicate very regularly with these organisations. I can reassure you that the TGA continually monitors and responds to medicine safety issues as they arise.

Thank you for your interest in medicines safety.

Yours sincerely

Adj. Professor John Skerritt
Health Products Regulation Group

23 July 2020

Adjunct Professor John Skerritt
Deputy Secretary, Health Products Regulation Group
Therapeutic Goods Administration (TGA)
PO Box 100
Woden ACT 2606

Dear Professor Skerritt

Thank you for your response to my letter of complaint. Your reply (dated 23 July 2020) provided general comments, however it did not address the specific TGA issues detailed in the *Prescribed Deaths – Life in the Killing Zone* report or my letter of complaint. As such I am compelled to ask you to provide a response that addresses the significant number of issues detailed in this letter and the report.

More importantly, I again urge you to take urgent action to address these issues.

TGA's role

The role of the TGA is to ensure all Australians are provided with the highest level of medication safety. The TGA is responsible for enforcing the *Therapeutic Goods Regulations 1990.*[i] The Statutory Rules No. 394, 1990 made under the *Therapeutic Goods Act 1989,* Schedule 12—Patient information documents (subregulation 9A(1)), requires the TGA to enforce the legal requirement that the CMI is consistent with the PI. The TGA must also ensure that information in the CMI meets the requirements as per the 'Patient information documents' section of the Act.

The TGA's 2018 opioid consultation paper titled *Prescription strong (Schedule 8) opioid use and misuse in Australia – options for a regulatory response* clearly demonstrated that the TGA's role and powers under the *Therapeutic Goods Act 1989* include the ability to require information in the PI to be included in a CMI. While the TGA does not have a role to approve each CMI, it has a clear role to ensure CMIs meet the legal requirements, with the ability to change the content.

Life-threatening risks not disclosed

The *Prescribed Deaths – Life in the Killing Zone* report shows that pharmaceutical companies breach TGA regulations by producing CMI documents that deliberately include misleading, inaccurate and incomplete information on the life-threatening risks of taking the medications. These breaches have been occurring for more than 20 years. These CMIs contain information that is not consistent with the PI and do not meet the requirements as per the 'Patient information documents' section of the Act.

In the report, we selected the group of opioids, benzodiazepines, codeine, antidepressants, antipsychotics and amphetamines for analysis, because they are classified as high-risk drugs on the PBS. They are commonly prescribed to people with disabilities, whose conditions and the side effects of the medication impact their cognitive ability. They are amongst our most vulnerable Australians.

The medications noted below offer a large sample to demonstrate the breadth of the issues (it is not an exhaustive list):

1. OxyContin
2. Endone
3. Valium
4. Xanax
5. Efexor

6. Lithium
7. Durogesic
8. Fluoxetine
9. Targin
10. Dexamphetamine
11. Panadeine Forte
12. Olanzapine
13. Clozapine
14. Nyxoid

The report focuses on the core role of the CMI to provide information on the risks associated with taking a medication. The Act requires details of these risks be included under the following areas:

- 3 – Advice before using the medicinal product (e.g. interactions, special warnings)
- 4 – How to use the medicinal product properly (e.g. withdrawal or other adverse effects)
- 5 – Further information (e.g. habit forming)
- 6 – Unwanted effects
- 7 – In case of overdose (e.g. symptoms and emergency procedures)

The *Prescribed Deaths – Life in the Killing Zone* report clearly identifies life-threatening risks associated with taking the PBS medications, including:

Death	**Addiction**	**Dependence**	**Withdrawal Syndrome**	**Overdose**
Respiratory Depression	**Abuse**	**Medicine Interaction**	**Alcohol Interaction**	**Coma**

The medications analysed are scheduled drugs due to these exact side effect risks, which are not being disclosed.

Reports from the ABS, AIHW, Department of Health, Penington Institute, and the National Drug and Alcohol Research Centre, also show that the medications analysed are the most common drugs found in adverse drugs events – hospitalisations, suicides and deaths – over the last 20 years.

Let me be clear that the report is focused on the cause of harm and death for thousands of Australians each year, many with severe disabilities, and the warnings that the CMI did not provide to them.

CMI and PI risks

You state that the CMI and PI are <u>not</u> required to contain exactly the same content, which I agree would be impractical. The report doesn't suggest that the breaches relate to all the risks not being included in the CMIs. Rather, the side effects analysed are narrowed to those that pose a risk of adverse drug events or death. I am sure you would agree that this information is the content that <u>must</u> be included for medications with this level of danger, given that scheduled drugs are commonly found in drug death toxicology screenings.

I highlight some comparative examples from the report that highlight the contradictory nature of information provided in CMIs and PIs:

- The Endone CMI describes the side effect of consuming alcohol whilst taking the medication as dizziness. In the PI the side effects listed include profound sedation, coma and death.

- The risks noted in the Valium PI but not the CMI include abuse, withdrawal syndrome, suicidal thoughts, fatal risks if combined with alcohol, life-threatening pregnancy and newborn risks, and death.
- The Valium PI also contains multiple warnings in relation to using a benzodiazepine with opioids – the leading cause of drug deaths in Australia. It states that the combined use should be avoided. It advises to prescribe the lowest dose for the shortest period of time if used together. It warns of the risk of overdose, respiratory depression, sedation, coma and death. The CMI does not even *mention* opioids once, nor the associated risks and warnings.
- The OxyContin PI describes the risks of an opioid overdose as respiratory depression, coma, and death, which are not included in the CMI.
- The Lithium CMI does not include the PI warning that lithium toxicity can result in coma and death. It also does not include the PI warnings that lithium toxicity can happen at prescribed doses, nor the risk of death from an overdose.
- The Dexamphetamine CMI states that using this medicine strictly as your doctor prescribed will ensure that abuse or drug dependence should not be a problem. The PI states that dependence and death can occur at prescribed doses.
- The risks included in the Panadeine Forte PI yet not mentioned in the CMI include death, addiction, dependence, tolerance, withdrawal and abuse. The CMI contains no mention of the life-threatening side effects of using this medication with alcohol or benzodiazepines. It also fails to mention that the medication is an opioid and a Schedule 4 drug. In total, we identified 14 breaches.
- The Prozac CMI does not include the life-threatening risk of serotonin syndrome, nor does it warn of the risk of death from an overdose.
- The Durogesic CMI does not include the PI warnings that addiction can occur in patients appropriately prescribed Durogesic at recommended doses. Nor is it noted that the risk of addiction is increased in patients with a mental illness or that the risk increases the longer the drug is used and with higher doses.

The report details many more examples of the systemic nature of the issue across multiple medication classes.

In your reply you state that the *CMI often describes more easily understood symptoms in lieu of the precise medical terminology*. That is not a valid reason to exclude life-threatening side effects from CMIs, which is what the report shows has occurred at a systemic level for decades. In addition, I am confident that consumers (and carers) will be able to easily understand the meaning of side effects like addiction, dependence, abuse, respiratory depression, overdose, coma, and death. These are specific examples of the side effect descriptions used in PIs but withheld from CMIs. Poignantly, these are also the descriptions of the risks that the TGA is requiring pharmaceutical companies to belatedly add to opioid CMIs.

A further question needs to be answered by the TGA. Based on the significant void of information included in historic and some current CMIs: do they actually meet the legal definition of a CMI?

Patient information

The report identifies multiple instances where CMI information is deliberately misleading, inaccurate or incomplete. These are also a breach of the 'Patient information documents' (subregulation 9A(1)) section of the Act. For example:

- The Endone CMI states, 'If abused it may become less able to reduce pain.' Endone is a Schedule 8 drug due to the risk of addiction, abuse and death. This warning completely fails to provide the TGA's position on the risks associated with abuse to the consumer.

- The OxyContin CMI states, '...many side effects tend to reduce over time, with the exception of constipation. This means that the longer you take this medicine, the less it may cause problems for you.' This warning for another Schedule 8 drug completely fails to provide the TGA's position on the long-term opioid side effect risks to consumers. This information was banned by the FDA soon after OxyContin was released.
- Valium (Diazepam) is another scheduled drug due to the risk of addiction, yet the CMI does not once mention the risk of addiction. Benzodiazepine addiction is a well acknowledged risk; even the government's healthdirect website states, 'If used over a long period, you can become addicted to diazepam.' [ii]Why isn't this information included in the CMI?
- Durogesic is fentanyl, an opioid and another Schedule 8 drug. The CMI states, 'If your pain continues, see your doctor who may prescribe additional medicines to help control the pain or change the dose of Durogesic. Your doctor may advise you initially to change the patch every two days (48 hours) instead of every three days (72 hours) to achieve adequate pain relief.' This information is dangerous and only a doctor should advise on the dosage of a medication.

Professor Skerritt, you assert that some risks are actually not required to be included in the CMI, and that directing a person to a discussion with their doctor or pharmacist is sufficient. Your explanation is that the inclusion of this information in the CMI would require a *high degree of medical literacy* to understand. I am unable to identify any legislative provision that suggests this should be the case for disclosing life-threatening side effects. The CMI has a role to explain side effects and that is what it must do; consistent with the PI. Explaining and understanding life-threatening risks in the PI may require a high degree of medical literacy, but the law requires they be explained in an easy to understand way in the CMI. *That is the purpose of the CMI*. The CMI already includes general advice for consumers to seek further information if required from a doctor or pharmacist.

Your reply to this point refers to the neonatal risks of Durogesic on page 109 as an example of when this is acceptable. This medication is widely acknowledged as one of the most lethal prescription medications. The neonatal risks in the PI that are not included in the CMI include respiratory depression, a life-threatening condition for a newborn. There is no justification for this warning to be excluded from the CMI. In any event, you appear to have overlooked that on page 244, the report details how these exact neonatal risks have now been added to the Durogesic Feb 2020 CMI. The language used is identical to the PI, so clearly the TGA believes consumers will understand it.

The *Therapeutic Goods Regulations 1990* require information be provided to consumers on 'warnings and precautions, such as when the medicine should not be taken' **and** warnings of the 'side effects' of taking a medication – these are separate requirements. Advising to not consume alcohol whilst taking the medication falls under 'warnings and precautions, such as when the medicine should not be taken.' Advising that the consumption of alcohol with the medication can result in respiratory depression, coma or death, is an explanation of potential 'side effects'.

The CMI analysis in the report shows the failure to provide the information on the side effects and medication interaction that is legally required.

Informed Consent

While I agree that the CMI is not a substitute for informed consent, it plays a role in the process. The CMI is the source of information on medication endorsed by the Australian Department of Health. It enables Australians to understand the side effects of a medication. This is a critical role in the informed consent process and millions of Australians rely on this information when taking a medication. Informed consent can only be legally valid if it is informed. The TGA has the role of ensuring the CMI delivers this information to consumers.

Yet the *Prescribed Deaths – Life in the Killing Zone* report details the systemic failings by the TGA in this role. In deciding to provide informed consent, a consumer is relying on a CMI that lacks all the material risks – so their consent is not informed. If the CMI does not replicate the description of risks provided by a doctor or pharmacist (and the TGA), then it has failed in its responsibility to support a patient making an informed decision. If the risks are not detailed, then they cannot be reinforced when a consumer reads the CMI at later times. The impact of the CMI not providing life-threatening side effect risks has legal implications that should not be easily dismissed.

TGA consumer warnings

The deadly irony of the CMI failings is that the TGA has released numerous consumer updates that include side effects not included in CMIs. For example, the report provides a detailed analysis of when life-threatening side effects for Panadeine Forte included in the PI have not been included in the CMI since 2000. The report shows that Panadeine Forte has been a common cause of drug deaths since its release.

In 2017, the TGA released a consumer fact sheet titled, *Codeine-containing medicines. Harms and changes to patient access. What's changing?* The fact sheet states:

> *"Some Australians don't realise how much harm codeine can cause."*
>
> *"Codeine is an opioid drug closely related to morphine and, like morphine, is derived from opium poppies. Codeine can cause opioid tolerance, dependence, addiction, poisoning and in high doses, death."*
>
> *"Severe withdrawal symptoms can result when the medicine is stopped."* [iii]

The reason why most Australians are unaware of the risks of codeine medications is that the CMIs have not included them. Panadeine Forte is a codeine medication. The CMI in 2017 did not mention this, nor the risk of opioid tolerance, dependence, addiction, poisoning and in high doses, death. The CMI also did not mention withdrawal symptoms. This has been the case since the 2000 CMI. The report also shows that the same risks were not included for Nurofen Plus, Tramadol, and Paracetamol and Codeine pain tablets.

Why did the TGA undertake a consumer awareness campaign on codeine medication without confirming that the CMIs for medications like Panadeine Forte contained information about these deadly side effects?

TGA industry briefing

Professor Skerrit, in November of 2017 you gave a health professionals presentation titled *Changes to codeine product access: background to the decision to change from over-the-counter to prescription only*. The Powerpoint presentation (which I accessed from the TGA website) detailed the history of death and adverse events due to codeine medication. It also outlined the issues relating to abuse, dependence, respiratory depression, death due to ultra-rapid metabolism, and contra-indicated the use of codeine in children aged 12–18 years post-adenotonsillectomy. [iv]

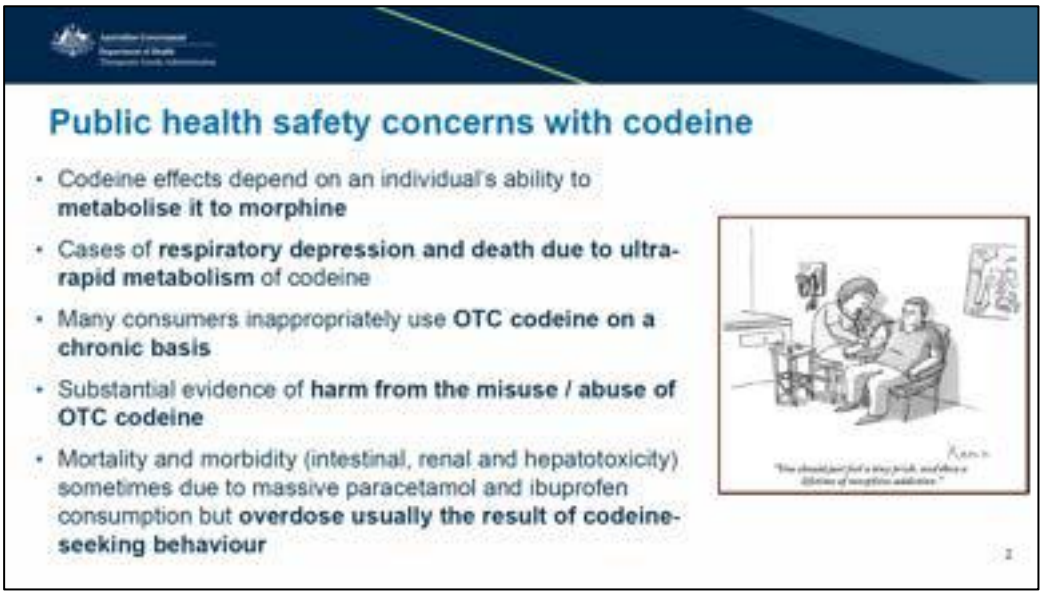
In the recording of the presentation, you discussed in detail the reasons for the changes, commenting:

> *"The babies have a rapid metaboliser gene and there's been deaths, for example, in North America for breastfed babies just with codeine turned into morphine in breast milk."*
>
> *"Codeine has and does kill people, and just a couple of the studies that mention codeine specifically in* Medical Journal of Australia*. 1437 codeine-related deaths and that is actually fairly old date of 2013. The numbers were going up when they stopped*

measuring, and while more people died from high dose opioids, the Oxycodone's and so forth, or Fentanyl, the numbers are still quite high for codeine. And so in their work, about 40% of the deaths they could attribute to either OTC or to prescription."

"Now again, it wasn't codeine alone, and it's very rare for someone just to be taking codeine alone. But as a trigger, so for example, alcohol codeine, benzodiazepines and codeine were in many of those cases so there is evidence of mortality with over the counter codeine."[v]

As with the 2017 TGA codeine fact sheet, none of these life threatening risks from your presentation were present in codeine CMIs including Panadeine Forte, Nurofen Plus, Tramadol, and Paracetamol and Codeine pain tablets. If they had been, then many of the 1437 people who died may still be alive.



Your presentation also included an illustration that highlighted the risk of iatrogenic addiction from the commencement of opioid medication. The risk of addiction at prescribed doses of medication is a significant problem. Monash University claim 50,000 new people become long-term users of dispensed pain killers each year, putting them at risk of addiction. Tragically this is another risk not disclosed in codeine medication and many other opioid CMIs.

Why did the TGA give a presentation to health professionals about codeine medication without confirming that the CMIs – that health professionals rely on for patient information – contained information about these deadly side effects?

New opioid CMIs

The report details the work of the TGA's opioid review, including the findings and the actions that are being taken. We included an analysis of the recent TGA review of the CMIs for opioid medications. Thankfully, warnings relating to coma, overdose, addiction, abuse and death are finally being included. The warnings that the TGA requires the pharmaceutical companies to add are the same side effects that the report identifies as information that should have already been in the CMIs. It is not new information based on recent scientific developments, as evidenced by FDA opioid warnings dating back to 2001. The changes now being made to CMIs are an emphatic admission of the opioid risks that should have already been declared in the CMIs, and how consumers have been exposed to deadly risks for decades.

Panadeine Forte

In my original letter of complaint, I included the issues relating to the Panadeine Forte CMI that was updated in May 2020[vi] by Sanofi-Aventis. Many risks have been added to the CMI as part of the TGA's review.

Incredulously, many life-threatening risks have still been withheld from the CMI, and yet these risks are detailed in the Panadeine Forte May 2020 PI[vii] that the TGA has approved for healthcare professionals. At a glance:

1. *Addiction*: The PI states that the risk of addiction is increased in patients with a personal or family history of substance abuse (including alcohol and prescription and illicit drugs) or mental illness. The comorbidity of mental illness and pain conditions is well known, so how can this warning not be included and highlighted in all opioid CMIs?
2. *Addiction*: The PI states that the risk also increases the longer the drug is used and with higher doses.
3. *Alcohol*: The PI warns of the risk of respiratory depression, coma and death when consuming alcohol.
4. *Overdose*: The PI warns of the risk of respiratory depression, coma, cardiac arrest and death if an overdose occurs, especially by children. The CMI does state that an overdose can occur at prescribed levels, making the need to explain the dangers of an overdose even more critical.
5. *CYP 2D6 gene*: The PI warns of the fatal risks of this medication to children who have the CYP 2D6 gene.
6. *Children*: The PI warns of the risk of death to children post tonsillectomy and/or adenoidectomy.
7. *Tolerance and Dependence*: The PI states the development of tolerance and physical dependence and risks of adverse effects, including hazardous and harmful use, that increases with the length of time a patient takes an opioid.
8. *Pregnancy*: The PI states that it may cause respiratory depression and withdrawal syndrome in neonates and newborn infants.
9. *Breastfeeding*: The PI warns of the risk of respiratory depression, morphine overdose and opioid toxicity and death for newborn infants.
10. *Opioid*: The PI states this medication is an opioid.

These risks are not included in the CMI and are clear instances of when the CMI is not consistent with the PI.

Subsequent to the report's release, we have further analysed the new Endone April 2020 CMI with the Endone April 2020 PI[viii] to identify further inconsistencies. Risks 1, 2, 3, 4, 8 and 10 as detailed for Panadeine Forte above, also apply to the Endone PI. Likewise, these risks are not included in the Endone April 2020 CMI, detailing areas in which the CMI is again not consistent with the PI.

This demonstrates that even after the TGA review of the CMIs, and the addition of new warnings, the systemic practice of withholding material risks from consumers continues.

Consumer updates

A large number of the changes to the new CMIs provide information that is the opposite to what was included in the previous CMIs. For example, the Durogesic CMIs (2018) and (1999) contain a statement that has no scientific basis: that the risk of addiction '…is *unlikely* when DUROGESIC is used correctly'. The current CMI (2020) now warns of the risk of addiction and death *even if* being taken correctly as prescribed.

The government program aimed at reducing adverse prescription medication deaths includes providing more warning information to consumers. The TGA has a stated objective to make these warnings more accessible to consumers. Yet the TGA has not made any change to the legal provision of CMIs. There is still no legal requirement for healthcare professionals, including pharmacists, to give a CMI to consumers even:

- when they first start a prescription
- on repeat prescriptions
- when new information on the risks of the medication are added to the CMI.

Based on the volume of conflicting and additional information contained in the new CMIs, which existing patients would not be aware of, why has the TGA not taken specific action to alert those Australians to these specific risks?

Why has the TGA not contacted each prescriber and pharmacy to require the provision of the new CMI on the next repeat or visit?

Why has the TGA not used media, social media and fact sheets to actively promote the exact risks and warnings that have been added to the CMI?

In 2018, after receiving a request from the Minister for Health, Greg Hunt, the TGA conducted a safety review of the asthma medication Montelukast (Singulair). The review was overseen by a panel including the TGA's chief medical advisor, Tim Greenaway, and yourself. The TGA then ordered manufacturers of Singulair to add warnings to the drug's CMI about its potential side effects, including suicidal thoughts. At the time, the TGA made no comment that these risks already existed in the Merck Sharp & Dohme Singulair October 2012 PI. The TGA then wrote to the manufacturers of Singulair requesting that CMI leaflets be included *inside* the drug's packaging. Why didn't the TGA do the same thing in 2020 for all new opioid CMIs?

The reality is that unless a consumer asks for a new CMI, there is no requirement for them to receive the updated warnings. The pharmacy visitation project within the report showed that pharmacists had no intention of providing the new CMIs. The Pharmacy Guild of Australia maintains the same position, which is a breach of their ethical obligations.

Failure to ensure that people are aware of these new warnings is a breach of the *Australian Charter of Healthcare Rights*, in which people can expect receive all information about the risks of medications.

The law of informed consent requires consent to be given when new risks for a medication are known. In addition to being informed of the new opioid risks, the consumer has to provide informed consent to continue to take the medication. Simply updating a CMI falls

horrifically short of what is required to ensure our basic human right to safe healthcare is being upheld by the TGA.

Nyxoid

The Minister for Health, Greg Hunt, announced that Nyxoid® (naloxone 1.8mg) nasal spray had been registered in Australia as an antidote to opioid overdose – it was placed on the PBS in November 2019. This medication is now a government-approved and government-funded emergency action for an opioid overdose. Its availability has been promoted by the Health Minister and the TGA as a key part of the program to reduce opioid deaths.

The 'Patient information documents' section of the Act requires a CMI to include, 'The action to be undertaken in the case of overdose (for example, symptoms and emergency procedures).' The report shows that opioid CMIs like Endone and Durogesic contain no mention of Nyxoid. It is not even included in the OxyContin and Targin CMIs, which are opioids made by the same maker of Nyxoid, Mundipharma.

Why has the TGA allowed these new opioid CMIs to exclude any reference to the opioid emergency rescue medication that the PBS is funding?

Self-harm and suicide

The statistics from the last 20 years show that the medication prescribed to treat mental illness and pain conditions are also the same medications used in suicide attempts and deaths. This includes benzodiazepines, antidepressants, opioids, analgesics and antipsychotics. These medications, and combinations of medications like opioids and benzodiazepines, are toxic enough to be classified as a lethal means of death.

The most common source of these medications is a person's usual doctor. It is common for these medications to be prescribed to a young person and or to a person who is at increased risk of self-harm. However, the CMIs for medications contain almost no information on the risk of medications being used in self-harm or suicides, nor does it provide any safety information that can be taken to reduce this risk. For example, the Prozac PI (2020) states:

> *During a 13-year period, there were 34 fatal reports of overdose where fluoxetine was the only reported ingestant.*

On the management of suicide risk, the PI states:

> *Prescriptions for PROZAC should be written for the smallest quantity of medicine consistent with good patient management, in order to reduce the risk of overdose.*

The Prozac CMI (2019) provides no warning of the risk of death from an overdose, and no warning to limit access to the medication supplies to prevent suicide attempts from an overdose.

Similarly, Olanzapine and Clopine (clozapine) CMIs contain no warning on the risk of death from an overdose. The report shows these three medications are commonly found in youth suicide attempts. The PIs for all medications state that overdoses can be fatal. Yet again, CMIs are inconsistent with the PIs.

Endep is a medication used for the treatment of major depression. The Alphapharm Endep Feb 2020 PI[ix] states:

> *"There is an increased risk of completed suicide by overdose with the 50 mg tablet compared with the 25 mg tablet. To prevent accidental overdose and the potentially fatal consequences, patients should be made aware of the unusual toxicity of tricyclic antidepressants and the need to maintain strict control over the tablets as well as the need to store them out of reach of children."*

"Deaths by deliberate or accidental overdosage have occurred with this class of medicine."

This is inconsistent with the Endep Feb 2020 CMI[x] which states:

"If you take too much Endep, you may feel drowsy, cold, very dizzy or have a fast or irregular heartbeat. You may also have fits, difficulty breathing or lose consciousness."

"Children are much more sensitive than adults to medicines such as Endep. An accidental overdose is especially dangerous in children."

The report details measures recommended by the WHO on high-risk medication, including having a family member store medications safely and dispense safe quantities as necessary – for instance keeping medication in a locked cabinet and only filling smaller prescription quantities at pharmacies. Reducing access to lethal means in the home, such as firearms and medication, can determine whether a person at risk for suicide lives or dies. The WHO also state that having lethal prescription medications in the possession of a person actually increases the risk of suicide, just like firearms.

The CMI is required to provide information on side effects, special risks, overdose and storage. Why has the TGA allowed the CMIs to include no warning of the risk of these medications being used in a deliberate overdose? Why has the TGA allowed the CMIs to contain no advice on the safe storage of these medications to reduce the risk of deliberate overdose? The lack of information in the CMIs fails to provide people with the ability to give informed consent to expose themselves to this risk.

These medications are legally prescribed and PBS-funded, and the TGA has allowed the CMIs to contain almost no consumer warnings to help patients and their families protect against the use of these drugs in self-harm and suicides.

Valium

Professor Skerritt, in November 2012 you replied to the Coroners Court of Victoria in relation to the findings of the *Inquest into the Death of David Andrew Trengrove*. Mr Trengrove was being treated for schizophrenia, depression and psychosis. His prescribed medications included MS Contin, Diazepam, Codeine/paracetamol, Alprazolam and Clonazepam. The coroner noted that there was no doubt that Mr Trengrove was addicted to the benzodiazepine medications. The coroner ruled that his death was the unintentional consequences of his intentional use and abuse of prescription medication.

The coroner report stated that there is a systemic public health issue of death associated with benzodiazepines, particularly when taken in combination with other central nervous system depressants such as opioid analgesics. The report also noted that benzodiazepines are present in around half of all Victorian drug deaths, including when they are combined with opioids. It further detailed that Diazepam was the second-most contributing individual drug in Victorian drug deaths in 2010.

The coroner's recommendation to the TGA was for a change to the scheduling from Schedule 4 to Schedule 8 for all benzodiazepines. This was recommended in order to reduce the harms, deaths, because of the addictive effects and the potential for abuse of benzodiazepines and opioids. The TGA did not support the recommendation, in part because of the information available to doctors about the quality, safety and effectiveness of benzodiazepines.

Your reply to Ms Kate Doherty, Coroners Registrar Coroners Court of Victoria, included a section titled ***Product Information / Consumer Medicine Information.*** The letter provided an analysis of the PI for a Diazepam, as well as attaching the full Roche Valium February 2010 PI[xi]. It noted that:

The PI also includes multiple Precautions about the use of this medicine. These include the advice that –

- *the risk of dependence increases with dose and duration of treatment;*
- *dependence is more pronounced in patients on long term therapy and/or high dosage and particularly so in predisposed patients with a history of alcohol or drug abuse;*
- *enhanced effects on sedation, respiratory depression and haemodynamic instability may occur when the medicine is co-administered with any centrally acting depressants, including narcotic analgesics.*[xii]

However, the Roche Valium February 2010 CMI[xiii] contains no mention of these risks. Other risks and warnings not detailed in this CMI include abuse, withdrawal syndrome, suicidal thoughts, fatal risks if combined with alcohol, life-threatening pregnancy and newborn risks, and death. The CMI does not even mention opioids once, nor the associated risks of overdose, respiratory depression, sedation, coma and death when combined with Valium. Your response to the coroner did not include a copy of the Roche Valium February 2010 CMI, only the PI. Nor did it provide an analysis of the CMI, only the PI. Professor Skerrit, why was this information on the Roche Valium February 2010 CMI not provided to the coroner ?

The letter simply stated that:

The CMI similarly contains information on the safe and effective use of medicines and are important because they provide information aimed at bringing about better health outcomes.

The analysis provided here and in the *Prescribed Deaths – Life in the Killing Zone* report emphatically rejects your statement in relation to Valium. The CMI did not provide Mr Trengrove with the legally required details on multiple life-threatening risks, and ten years later the Valium CMI still doesn't. According to the Penington Institute overdose report, for the period 2001–2012, benzodiazepines were involved in 4,159 accidental deaths. Having analysed the lack of warnings in the CMIs, it is easy to see how this happened.

Alprazolam

Two years later, Alprazolam was rescheduled in February 2014 from a Schedule 4 to a Schedule 8 controlled drug. The reasons for the decision given by the TGA included that in comparison to other benzodiazepines, Alprazolam has increased morbidity and mortality in overdose with possible increased toxicity. There had been a rapid increase in use of Alprazolam compared with other benzodiazepines and evidence of widespread misuse. There was also evidence of abuse and misuse with opioids. Studies by the National Drug & Alcohol Research Centre indicated higher rates of addiction and abuse in comparison to other benzodiazepines like Valium.

On 31 July 2020 the Apotex GenRx Alprazolam October 2015 CMI[xiv] was downloaded from the TGA website. It has been six years since this medication was rescheduled to a controlled drug and five years since this CMI was updated. Despite this extraordinary length of time, the current CMI contains no mention of:

- risk of abuse
- risk of addiction
- risk that dependence increases with higher doses and long-term use
- risk of withdrawal symptoms
- risk of respiratory depression, coma or death if combined with opioids
- risk of respiratory depression, coma or death if combined with alcohol
- risk of respiratory depression, coma or death from overdose
- risk of suicide
- risk of life-threatening pregnancy and breastfeeding conditions.

It is difficult to understand how a medication that was rescheduled due to the risk of death contains no mention of death at all in the CMI. Likewise, the absence of information about the risk of abuse alone and in combination with opioids. Needless to say, the CMI is inconsistent with the Apotex GenRx Alprazolam October 2015 PI[xv].

Similar issues were found with other Alprazolam CMIs downloaded on 31 July, including the Aspen Alprazolam March 2017 CMI[xvi] and Genepharm Alprazolam CMI, which has not been updated since July 2009[xvii]!

TGA and FDA

Your letter response states that *TGA standards are aligned with those employed by other medicines regulators including the FDA and the EMA, and we collaborate and communicate very regularly with these organisations*.

Chapter 2 of the *Prescribed Deaths – Life in the Killing Zone* report provides a detailed analysis of when the risk of death is not mentioned as a potential side effect in a CMI, yet it is included in the comparable FDA Medication Guide (MG). You would be aware that the FDA included these risks in the MGs more than 15 years ago. Knowing that these risks have been included by the FDA for each medication and side effect listed, it is a failure that the TGA did not require these risks to be included in the CMIs for Australians.

For example:

> **OxyContin FDA vs TGA *consumer information***
>
> **Purdue (US) – Addiction**: A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. *Even if* you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death.
>
> **Mundipharma (Aus) – Addiction**: There is *potential* for abuse of oxycodone and the development of addiction to oxycodone.

The FDA approves the content of all warning labels and documents. This includes consumer warnings, side effects and drug interaction guides. The FDA advises pharmaceutical companies of any changes that need to be made and the final version requires FDA sign off before being used. The report details that the FDA requires that MGs be issued with each dispensing of medications comparable to Schedule 4 and 8 drugs in Australia.

Unlike the FDA, the TGA neither approves each CMI nor do you require a CMI to be provided with each prescription. The TGA only requires these be 'available', meaning it can be provided but not that it must be provided. It is not even mandatory to provide a CMI for medications deemed 'dangerous' by the TGA, including Schedule 4 or 8 drugs.

These are medications with significant side effects including the risk of overdose, addiction and death. Access to these drugs is restricted because they are dangerous but the access to the CMI is typically reliant on the consumer asking for it.

Each CMI contains the advice to *Keep this leaflet with the medicine. You may need to read it again*, yet the consumer would only receive it if they ask.

When it comes to the TGA standards for consumer warnings, the TGA is not even remotely aligned to the FDA or what is required to ensured consumers receive the warnings that can save a life.

New CMIs

Your response states that a *new format will be implemented for all new medicines that require a CMI from the start of next year and adopted other medicines within a set transition period*. The format is important, but it is the content that is critical.

The opioid CMIs now contain warnings that combining them with other medications like benzodiazepines, other pain relievers, antidepressants, and antipsychotics, may result in severe drowsiness, decreased awareness, breathing problems, coma and death. There is no information on what changes will be made to the risks included in the new non-opioid CMIs and if risks like these will be added.

The TGA has shown no urgency to include these warnings in the non-opioid medications for Schedule 4 and 8 drugs, which is simply unfathomable.

Opioid Crisis

Your reply states that you can reassure me *that the TGA continually monitors and responds to medicine safety issues as they arise*.

The report details that the increase in opioid deaths escalated in line with the TGA allowing greater scope for doctors to prescribe stronger opioids like OxyContin for moderate pain in 2000. The TGA failed to ensure that the life-threatening risks were included opioid CMIs in 2000, as detailed in Chapters 2 and 11. The original OxyContin CMI in 2000 did not mention the risk of death once, a medication that had already proven to be a deadly opioid in the US since 1996, causing the opioid epidemic.

ABS data shows deaths relating to OxyContin commenced following its release in 2000 and rapidly increased over time. Mundipharma has produced OxyContin CMIs since 2000 that have placed Australians at greater risks of adverse drug events and death – and still do. Yet 20 years later and the TGA has still not taken legal action against Mundipharma for the resulting impact on human life that is directly attributed to the CMIs they produced.

Chapter 8 of the report provides a detailed comparison of the USA opioid crisis and the medications attributed as the cause: OxyContin and Durogesic. It also details the FDA response commencing in 2001 and includes successful court action against Purdue in 2007 for deliberately misleading the true material risks associated with OxyContin, including the risks of addiction and abuse. It is impossible to comprehend why the TGA did not investigate Mundipharma back in 2001 and 2007. Perhaps an investigation would have resulted in the CMIs being corrected and lives saved. Even when Mundipharma released its 'abuse resistant' formulation in 2014, the TGA still did not require the new CMI to include the risk of abuse that still exists. Even now, the OxyContin CMI has still not been updated in line with the new opioid CMI changes.

Human Rights

The rights of vulnerable people – in fact, all people – to safe healthcare is enshrined in the Universal Declaration of Human Rights, the Australian Charter of Healthcare Rights, and the Convention on the Rights of Persons with Disabilities.

It is a legal requirement that people are provided with accurate, up-to-date information on the risks of all medications. This includes when multiple medications are prescribed. The TGA has failed to uphold the rights of persons with disabilities to information, which impacts our ability to exercise our legal right to informed consent and most tragically fails to uphold our right to the highest attainable standard of health. You simply cannot assess a risk that you don't know about. You cannot follow safety advice if it has never been given to you. Protecting vulnerable Australians does not appear to be as important to the TGA as investigating sporting apparel that claims to protect against COVID-19.

Urgent action is required

The *Prescribed Deaths – Life in the Killing Zone* report has documented multiple medication safety failures, across multiple classes of medication. The report also proposes a number of recommendations to immediately stop adverse prescription drug events and deaths being suffered by too many Australians.

The urgency of this matter cannot be understated. The current global health crisis has seen an increase in the number of Australians seeking help for mental health conditions.

There are 16 million opioid and 6 million benzodiazepine prescriptions filled each year. Australia is the second highest user of antidepressants in the world. The prescribing of these medications has dramatically escalated in 2020 through telehealth consultations. Australians have never been more exposed to the side effects of the drugs.

The *Australian Financial Review* reported in July 2020 that data collected from GPs across Melbourne and Sydney showed a sharp rise in new mental health diagnoses in 2020, with numbers rising every week since the end of April (compared to 2019 figures). Anxiety makes up a significant portion of new diagnoses, while mental health issues in Sydney also spiked during the summer bushfires.

The data showed a substantial increase in the prescription of anti-depressants by GPs – up to a 31 per cent increase in prescription of some anti-anxiety drugs and up to a 46 per cent increase in some anti-psychotics. [xviii]

Urgent action is required to ensure all existing users of these medications are made aware of the risks not previously disclosed, and new users must have all the risks made available to them.

Restating my formal complaint

Professor Skerritt, opioids, benzodiazepines, codeine, antidepressants, antipsychotics, mood stabilisers and amphetamines are medications that have been prescribed to me since 2012. The risks that have not been included in the CMIs are risks that I have been exposed to, risks that have impacted my health and nearly cost me my life on two occasions. I have always been prescribed polydrug treatments – at least two and as many as seven medications at the same time. This complaint is not only about systemic issues that exist with medication safety, it is also a complaint to the TGA about my personal adverse drug experiences with these medications. I can assure you that my commitment to this complaint will continue until the TGA takes the required action. That action is detailed in section 4.2 on page 349 of the report, however I am prepared to discuss this further with yourself.

The issues examined in the report demonstrate that Australians like me will continue to be exposed to further adverse health events caused by systemic failures by the TGA to provide safe healthcare if action is not taken.

Regards

Patrick O'Connor

[redacted]

4 August 2020

CC: Commonwealth Ombudsman, Ref: 2020-708611
CC: Royal Commission into Violence, Abuse, Neglect and Exploitation of People with Disability, Ref: RC. SUB.001.00367
CC: Royal Commission into Aged Care Quality and Safety, Ref: AWF.001.05346

Note: all references to data in this letter are contained in the *Prescribed Deaths – Life in the Killing Zone* except for those provided below.

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[i] Australian Government, *Therapeutic Goods Regulations 1990*, Compilation No. 77, 1 July 2017.
[ii] healthdirect website, accessed on 28 July 2020, see https://www.healthdirect.gov.au/diazepam
[iii] Australian Government Department of Health Therapeutic Goods Administration, *Codeine-containing medicines. Harms and changes to patient access*, fact sheet, un-dated.
[iv] Australian Government Department of Health Therapeutic Goods Administration, *Presentation: Changes to codeine product access: background to the decision to change from over-the-counter to prescription only*, Codeine up-scheduling workshop, Melbourne, 28 November 2017, published 16 January 2018, see https://www.tga.gov.au/node/768885
[v] ibid.
[vi] Sanofi Aventis Panadeine Forte May 2020 CMI
[vii] Sanofi Aventis Panadeine Forte May 2020 PI
[viii] Aspen Endone April 2020 PI
[ix] Alphapharm Endep Feb 2020 PI
[x] Alphapharm Endep Feb 2020 CMI
[xi] Roche Valium February 2010 PI
[xii] Australian Government Department of Health Therapeutic Goods Administration, letter to Ms Kate Doherty, Subject: Investigation into the death of David A Trengrove, 6 November 2012.
[xiii] Roche Valium February 2010 CMI
[xiv] Apotex GenRx Alprazolam October 2015 CMI
[xv] Apotex GenRx Alprazolam October 2015 PI
[xvi] Aspen Alprazolam March 2017 CMI
[xvii] Genepharm Alprazolam July 2009 CMI
[xviii] Callaghan, R, 'Mental health toll reflected in diagnoses, drug prescriptions', *Australian Financial Review*, 14 July 2020.

Australian Government
Department of Health
Therapeutic Goods Administration

Codeine-containing medicines

Harms and changes to patient access

What's changing?

From 1 February 2018, medicines that contain codeine will no longer be available without prescription.

Your pharmacist will be able to help you choose from a range of effective products that do not require a prescription. If you have strong or chronic (long-lasting) pain you will need to consult your doctor, and if medicines are part of your treatment, a prescription may be needed.

Why is access to codeine changing?

Some Australians don't realise how much harm codeine can cause.

Most Australians are unaware that over-the-counter medicines containing codeine for pain relief offer very little additional benefit when compared with medicines without codeine. The use of such medicines, however, is associated with high health risks, such as developing tolerance or physical dependence on codeine.

Codeine is an opioid drug closely related to morphine and, like morphine, is derived from opium poppies. Codeine can cause opioid tolerance, dependence, addiction, poisoning and in high doses, death.

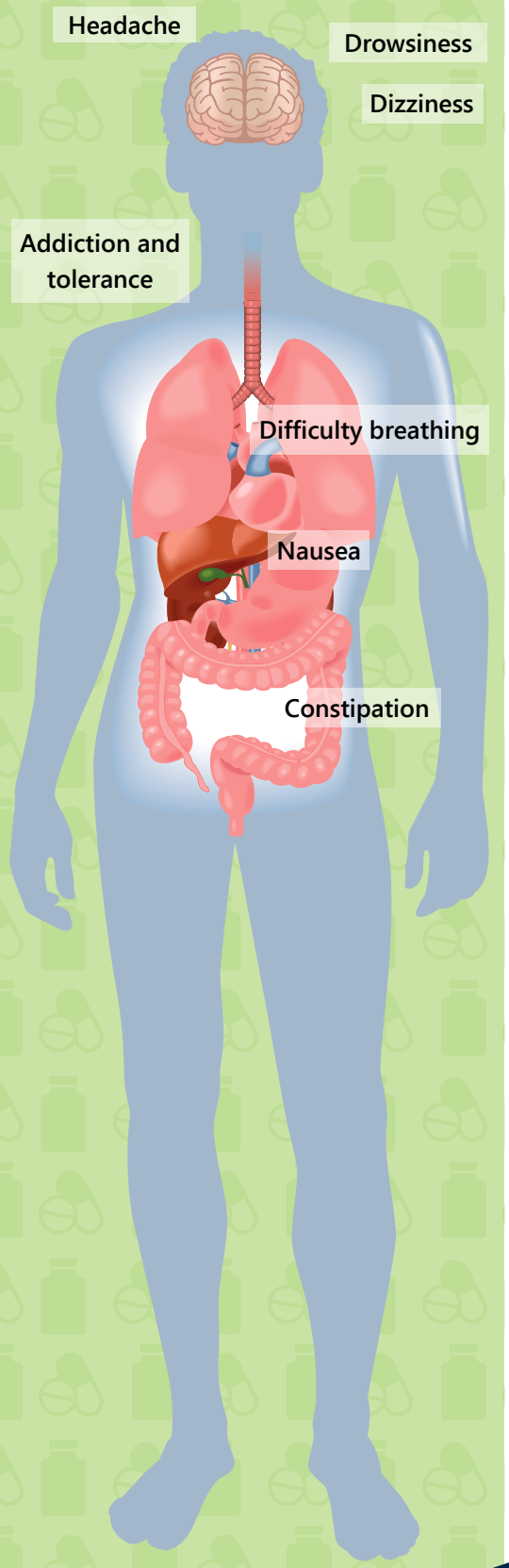
Codeine use can be harmful

Tolerance occurs when codeine becomes less effective and so the body needs higher and higher doses to feel the same relief from your symptoms. **Severe withdrawal symptoms** can result when the medicine is stopped; these include **head and muscle aches, mood swings, insomnia, nausea and diarrhoea**. Some of these withdrawal symptoms, such as head or muscle aches mimic the symptoms that low-dose codeine products are often used to treat, leading to people incorrectly continuing to take the medicine longer or in higher doses.

Codeine poisoning contributes to both accidental and intentional deaths in Australia. The codeine-containing medicines that are currently available over-the-counter are usually combined with either paracetamol or ibuprofen. Regular use of medicines containing codeine, for example for chronic pain, has led to some consumers becoming addicted or tolerant to codeine without realising it. Taking more than the recommended dose of combination products could result in serious side effects. Though safe at recommended doses, long term use of high doses of paracetamol can result in **liver damage** while the most severe adverse effects of long term ibuprofen use include serious **internal bleeding, kidney failure** and **heart attack**.

Codeine use can lead to tolerance, dependence, addiction, poisoning and even death

Major symptoms include:



Codeine is also sometimes used in medicines to relieve the symptoms of cough and cold, however there are safer and more effective medicines available that may provide relief from these conditions. Talk to your pharmacist or doctor for advice on what may be best for you.

How and where to get advice

Pharmacists have an important role to play in minimising harm from codeine.

The current range of codeine-containing over-the-counter medicines will continue to be available without a prescription in pharmacies until 31 January 2018. Pharmacists will continue to be an important source of information and advice for consumers both before and after this date.

Most people should be able to manage acute pain or cough and cold symptoms with safer medicines. For acute pain, this may include products containing paracetamol or ibuprofen, or the two products in combination. Your pharmacist will be able to provide advice on the most appropriate medicines for you. Speaking with your pharmacist is particularly important if you have any other medical conditions, such as stomach, kidney, liver or heart problems.

Talk to your doctor

People with ongoing pain should talk to their doctor or healthcare provider to determine better alternative treatment options. These may include: alternative over-the-counter or prescription medicines; non-medicine therapies from an allied health professional such as a physiotherapist; self-management tools such as exercise or relaxation; or referral to a pain specialist or pain management clinic.

Ask your doctor about a Medicare-funded care plan which will allow you access to a rebate for treatment from an allied health professional. Medicare provides a rebate for the preparation of a Chronic Disease Management Plan and a Team Care Arrangement. For more information see www.health.gov.au/internet/main/publishing.nsf/content/mbsprimarycare-chronicdisease-pdf-infosheet.

If you think that you are unable to manage without codeine and experience some of the side effects of withdrawal talk to your doctor about getting help.

Next steps

A Nationally Coordinated Codeine Implementation Working Group (NCCIWG) has been established with representatives from state and territory health departments and peak professional bodies representing consumers, pharmacists and medical professionals. The purpose of this working group is to assist with the implementation of a communication strategy to help inform the community of the upcoming changes to the availability of low-dose codeine containing medicines from 1 February 2018.

Advice for pharmacists and medical professionals regarding the changes to codeine access and to help them provide the best advice to their patients will be made available on the Department's website at www.health.gov.au.

For more information and support:

NPS MedicineWise
www.nps.org.au

Alcohol and Drug Information Service (ADIS)
www.drugs.health.gov.au

Pain Australia
www.painaustralia.org.au

Chronic Pain Australia
www.chronicpainaustralia.org.au

painHEALTH
https://painhealth.csse.uwa.edu.au

Australian Pain Management Association
www.painmanagement.org.au

Ask Your Pharmacist:
askyourpharmacist.com.au

Pain Management Network
www.aci.health.nsw.gov.au/chronic-pain

Pain Link Helpline
1300 340 357

Healthdirect Australia - 24 Hour Health Advice Line: 1800 022 222

Contact information for state and territory drugs and poisons units

ACT Health
Pharmaceutical Services: www.health.act.gov.au/public-information/businesses/pharmaceutical-services

NSW Ministry of Health
Pharmaceutical Services: www.health.nsw.gov.au/pharmaceutical/Pages/default.aspx

NT Department of Health
Environmental Health – Medicines and Poisons Control: https://health.nt.gov.au/professionals/environmental-health/medicines-and-poisons-control

QLD Health
Medicines Regulation & Quality Unit: www.health.qld.gov.au/clinical-practice/guidelines-procedures/medicines
Poisons Management: www.health.qld.gov.au/system-governance/licences/medicines-poisons/poisons-management

SA Health
Medicines and Technology Policy and Programs: www.sahealth.sa.gov.au/MTPP

TAS Department of Health & Human Services
Pharmaceutical Services: www.dhhs.tas.gov.au/psbtas/welcome

VIC Department of Health & Human Services
Drugs and Poisons Regulation: www.health.vic.gov.au/dpu/

WA Health
Pharmaceutical Services: www.public.health.wa.gov.au/1/872/2/pharmaceutical_services.pm

VALIUM®

pronounced (val-i-um)

contains the active ingredient diazepam

Consumer Medicine Information

What is in this leaflet

This leaflet answers some common questions about VALIUM.

It does not contain all the available information.

It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you taking VALIUM against the benefits they expect it will have for you.

If you have any concerns about taking this medicine, ask your doctor or pharmacist.

Keep this leaflet with the medicine.

You may need to read it again.

What VALIUM is used for

VALIUM is used for anxiety. Anxiety or tension associated with the normal stress of everyday life usually does not require treatment with medicines.

VALIUM is used to relax muscles.

VALIUM can also be used to treat trembling, confusional states or anxiety associated with alcohol withdrawal. It is also used to treat panic attacks.

VALIUM belongs to a group of medicines called benzodiazepines. They are thought to work by their action on brain chemicals.

Benzodiazepines are not recommended as the only treatment of severe mental illnesses and should not be used alone to treat depression.

Your doctor, however, may have prescribed VALIUM for another purpose.

Ask your doctor if you have any questions about why VALIUM has been prescribed for you.

In general, benzodiazepines such as VALIUM should be taken for short periods only (around 2 to 4 weeks). Continuous long term use is not recommended unless advised by your doctor.

The use of benzodiazepines may lead to dependence on the medicine.

This medicine is available only with a doctor's prescription.

Before you take VALIUM

Do not take VALIUM if:

1. **you have had an allergic reaction to VALIUM, any other benzodiazepine medicine or any ingredients listed at the end of this leaflet**
2. **you have severe and chronic lung disease**
3. **you have severe liver disease**
4. **you have temporary stops in breathing during sleep**
5. **you suffer from severe muscle weakness**
6. **you have drug or alcohol addiction**
7. **the packaging is torn or shows signs of tampering**
8. **the expiry date (EXP) printed on the pack has passed.**

   If you take this medicine after the expiry date has passed, it may not work as well.

If you are not sure whether you should be taking VALIUM, talk to your doctor.

Do not give VALIUM to children less than six months old.

Before you start to take it:

Your doctor must know about all the following before you start to take VALIUM.

1) if you are pregnant or plan to become pregnant

It is not known whether VALIUM is harmful to an unborn baby when taken by a pregnant woman. If there is a need to take VALIUM when you are pregnant your doctor will discuss the risks and benefits to you and the unborn baby.

2) if you are breastfeeding or plan to breastfeed

VALIUM may pass into the breast milk and cause drowsiness and/or feeding difficulties in the baby. VALIUM is not recommended for use while breastfeeding.

3) if you have any other health problems including:

- liver, kidney or lung disease
- high or low blood pressure
- glaucoma (high pressure in the eye)

- depression, schizophrenia or other mental illness
- epilepsy (fits)

4) if you drink alcohol

Alcohol may increase the effects of VALIUM.

5) if you are allergic to any other medicines, foods, dyes or preservatives.

Taking other medicines

Tell your doctor if you are taking any other medicines including any that you have bought without a prescription from a pharmacy, supermarket or healthfood shop.

Some medicines may interfere with VALIUM. These medicines include:

- other sleeping tablets, sedatives or tranquillisers
- medicines for depression
- medicines to control fits
- medicines for allergies or colds eg. antihistamines
- pain relievers
- muscle relaxants
- cimetidine and omeprazole- a medicine used to treat ulcers
- disulfiram - a medicine used in alcohol abuse
- cisapride-a medicine used to treat gastric reflux
- ketoconazole- a medicine used to treat fungal infections

These medicines may be affected by VALIUM or may affect how well VALIUM works. Your doctor or pharmacist can tell you what to do if you are taking any of these medicines. They also have a more complete list of medicines to be careful with or avoid while taking VALIUM.

If you are taking any other medications, check with your doctor before you start to take VALIUM.

How to take VALIUM

How much to take

Take VALIUM exactly as your doctor has prescribed.

Your doctor will tell you how many VALIUM tablets to take each day.

The dose varies from person to person depending on age and the condition being treated. The usual adult dose is between 5 and 40 mg daily. Children , elderly and very ill patients may need to take less.

How to take it

Tablets should be swallowed whole with a glass of water.

When to take it

Valium can be taken up to three times a day. Your doctor will tell you how much you need to take. The tablets can be taken with or without food.

How long to take VALIUM

Usually, VALIUM should be taken for short periods only (for example, 2-4 weeks). Continuous long term use is not recommended unless advised by your doctor. The use of benzodiazepines may lead to dependence on the medicine.

Continue taking VALIUM until your doctor tells you to stop.

If you forget to take VALIUM

If it is almost time for your next dose, skip the dose you missed and take your next dose when you are meant to. Otherwise, take it as soon as you remember and then go back to taking it as you would normally.

Do not double a dose to make up for one you have missed.

If you are not sure whether to skip the dose, talk to your doctor or pharmacist.

In case of an overdose

Immediately telephone your doctor or Poisons Information Centre (telephone 13 11 26) for advice or go to Accident and Emergency at your nearest hospital if you think that you or anyone else may have taken too much VALIUM, even if there are no signs of discomfort or poisoning.

You may need urgent medical attention.

Keep telephone numbers for these places handy.

If you have taken too much VALIUM, you may feel drowsy, tired, confused, dizzy, have difficulty breathing, feel weak or become unconscious.

If you are not sure what to do, contact your doctor or pharmacist.

While you are taking VALIUM

Things you must do

Tell all doctors, dentists and pharmacists who are treating you that you are taking VALIUM.

Do not take any other medicines whether they require a prescription or not without first telling your doctor.

Tell your doctor if you become pregnant while taking VALIUM.

Tell your doctor if, for any reason, you have not taken your medicine exactly as prescribed.

Otherwise, your doctor may think that it was not effective and change your treatment unnecessarily.

Tell your doctor if you feel the tablets are not helping your condition.

Be sure to keep all of your appointments with your doctor so that your progress can be checked.

Things you must not do

Do not drive or operate machinery until you know how VALIUM affects you.

VALIUM may cause drowsiness or dizziness in some people and therefore may affect alertness. Make sure you know how you react to VALIUM before your drive a car or operate machinery or do anything else that could be dangerous if you are drowsy, dizzy or not alert.

Do not take VALIUM for a longer time than your doctor has prescribed. VALIUM should be taken for short periods only (for example 2 to 4 weeks) unless advised by your doctor.

Do not stop taking VALIUM or lower the dose without first checking with your doctor. Stopping this medicine suddenly may cause some unwanted effects. Your doctor will explain how you should slowly reduce your dose of VALIUM before you can stop taking it completely.

Do not let yourself run out of medicine over the weekend or on holidays.

Do not suddenly stop taking VALIUM if you suffer from epilepsy. Stopping this medicine suddenly may make your epilepsy worse.

Do not give VALIUM to anyone else even if their symptoms seem similar to yours.

Do not use VALIUM to treat other complaints unless your doctor says to.

Things to be careful of

Be careful when drinking alcohol while taking VALIUM.

Combining VALIUM and alcohol can make you more sleepy, dizzy or lightheaded. Your doctor may suggest that you avoid alcohol or reduce the amount of alcohol you drink while you are taking VALIUM.

Be careful if you are elderly, unwell or taking other medicines.

Some people may experience side effects such as drowsiness, confusion, dizziness and unsteadiness which may increase the risk of a fall.

Side Effects

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking VALIUM.

VALIUM helps most people with anxiety but it may have unwanted side effects in a few. All medicines can have side effects. Sometimes they are serious, most of the time they are not. Some side effects may require medical treatment.

Ask your doctor or pharmacist to answer any questions you may have.

Tell your doctor if you notice any of the following and they worry you:

- drowsiness, tiredness
- dizziness, unsteadiness
- loss of memory, inattentiveness, confusion, lack of concentration
- headache, hangover feeling in the morning
- slurred speech
- unpleasant dreams

Tell your doctor immediately or go to casualty at your nearest hospital if you notice any of the following:

- sudden anxiety or excitation
- restlessness, agitation, irritability, anger, abnormal behaviour
- hallucinations or delusions
- severe sleep disturbances
- difficulties in breathing or choking or coughing

These are serious side effects. You may need urgent medical attention. Serious side effects are rare.

This is not a complete list of all possible side effects. Others may occur in some people and there may be some side effects not yet known.

Tell your doctor if you notice anything else that is making you feel unwell, even if it is not on this list.

Ask your doctor or pharmacist if you don't understand anything in this list.

Do not be alarmed by this list of possible side effects. You may not experience any of them.

After taking VALIUM

Storage

Keep your tablets in the original packaging until it is time to take them.

If you take the tablets out of the blister pack they may not keep well.

Keep VALIUM in a cool dry place where the temperature stays below 30°C.

Do not store it, or any other medicine, in a bathroom or near a sink.

Do not leave it in the car or on window sills.

Heat and dampness can destroy some medicines.

Keep VALIUM where children cannot reach it.

A locked cupboard at least one-and-a-half metres above the ground is a good place to store medicines.

Disposal

If your doctor tells you to stop taking VALIUM, or the medicine has passed its expiry date, ask your pharmacist what to do with any tablets that are left over.

Product Description

What VALIUM looks like

VALIUM 2 mg Tablets are round, white with a score break and Roche 2 on one side.

VALIUM 5 mg Tablets are round, yellow with a score break and Roche 5 on one side.

Ingredients

Active ingredient -

diazepam

each 2 mg tablet contains 2 mg diazepam

each 5 mg tablet contains 5 mg diazepam

Inactive ingredients -

both 2 mg and 5 mg tablets contain lactose, maize starch and magnesium stearate (470).

the 5 mg tablets also contain the colouring iron oxide yellow, CI 77492 (172)

VALIUM tablets are gluten free

VALIUM 2 mg Tablets come in packs of 50.

VALIUM 5 mg Tablets come in packs of 50.

Manufacturer

VALIUM is distributed by:

Roche Products Pty Limited

ABN 70 000 132 865

4 - 10 Inman Road

Dee Why NSW 2099

AUSTRALIA

Customer enquiries: 1 800 233 950

Please check with your pharmacist for the latest Consumer Medicine Information.

Australian Registration Number

- VALIUM 2 mg Tablets
  AUST R 66129
- VALIUM 5 mg Tablets
  AUST R 48566

This leaflet was prepared on 18 February 2010

Office of the Deputy Secretary
Adjunct Professor John Skerritt
Therapeutic Goods Administration
PO Box 100
Woden ACT 2606

Professor Skerritt

I have not received a response to my letter dated the 4th August. I have also reviewed your reply to Shane Rattenbury MLA dated 22nd September and will incorporate my views on that in this letter.

Consumer Medicines Information (CMI)

The core reason for my complaint is that medically acknowledged risks and side effects, known to the TGA, have not been included in the CMIs for a wide range of high-risk PBS medications. The side effects and risks include death, addiction, dependence, withdrawal symptoms, coma, pregnancy complications, overdose, drug to drug interactions and abuse. Australians are not aware of these risks, and they are not able to take the necessary steps to avoid adverse drug events and death. The medications researched include benzodiazepines, antidepressants, antipsychotics, opioids, codeine, and mood stabilisers. They are Scheduled drugs due to the risks, which are not included in the CMIs.

The CMI is the medication information resource provided by the Australian Department of Health to educate and remind people of the warnings needed to prevent medication related harm and death. The document is only as useful as the information it contains, it can only save lives if it contains lifesaving information! Your role as the regulator, is to ensure it contains this vital information. My complaint details how the TGA has failed to do this and asks for urgent action.

The Penington Institute shows that drug deaths happen to everyday Australians taking medications like Valium, Ativan, Panadeine Forte, and Prozac. The medications that are causing these deaths are the *same ones that have the absence of life saving warnings in the CMI*, there is a clear cause and effect link. A person cannot assess a risk that they do not know about nor follow safety advice if it has not been provided.

Pharmaceutical medications linked to deaths in 2018:

1. Benzodiazepines (e.g. Valium) **899 deaths**
2. Opioids (e.g. Endone, Panadeine Forte) **647 deaths**
3. Anti-depressants (e.g. Prozac) **591 deaths**
4. Anti-psychotics (e.g. Lithium) **318 deaths**
5. Anti-convulsants (e.g. epilepsy meds) **174 deaths**

Source: Penington Institute Annual Overdose Report 2020. Figures are preliminary and are expected to rise.

In your response to Minister Rattenbury and myself, you fail to acknowledge and address the specific side effects and risks, that I have detailed are **not** included in the CMIs. Hence, I am compelled to again ask for a comprehensive response to the individual CMIs analysed in all my communications with your office, including the *Prescribed Deaths* report.

More importantly I call on you to urgently take the following action; any serious risk or side effect that could adversely impact a person's health or cause death that is acknowledged by the TGA and the Department of Health, to be adequately explained in the CMI and all existing users warned. This includes any life-threatening risk or side effect that the manufacturer discloses in the Product Information that has been approved by the TGA. Providing this information in written form is a right under the Universal Declaration of Human Rights, the Australian Charter of Healthcare Rights, the Law of Informed Consent, and the Convention on the Rights of Persons with Disabilities.

Benzodiazepines

Schedule 12 of the *Therapeutic Goods Regulations 1990* states that a CMI must include information on contraindications, precautions for use, interactions with other medicines and alcohol, special warnings, withdrawal or other adverse effects, habit forming potential, symptoms of overdose, and undesirable/unwanted effects that can occur.

The failure of the TGA to ensure CMIs contain the required information is highlighted in the analysis of benzodiazepine CMIs. Within these CMIs, the most critical failure relates to the risks when taking a benzodiazepine with an opioid or alcohol. RACGP Benzodiazepine Guidelines[i] state:

"When benzodiazepines are combined with other CNS depressants (eg alcohol, opioids), patients are at risk of respiratory depression, heavy sedation, coma and death."

The Department of Veteran Affairs warns that the risk of death for a person taking an opioid and a benzodiazepine is 15 times greater than that for a person not taking these medications, which occurs even at prescribed doses[ii].

The deadly lack of information in benzodiazepine CMIs is highlighted in the comparison of the warnings for these risks between the Valium CMI for consumers and the Valium Product Information that is provided to health care professionals and approved by the TGA.

Product Information – side effects of combining Valium with alcohol or opioids	CMI – side effects of combining Valium and alcohol	CMI – side effects of combining Valium and opioids
"...severe sedation that could result in coma or death, clinically relevant respiratory and/or cardiovascular depression."	"...drowsiness, confusion, dizziness and unsteadiness which may increase the risk of a fall."	Opioids have never been included in any Valium CMI since 2000

Studies from La Trobe University show that the concurrent use of opioid and benzodiazepine medication is common in Australia. One study of PBS data concludes that over a 4-year period ending December 2016, *760,000 individuals were dispensed both opioids and benzodiazepines on the same day!* The most common opioids were codeine (e.g. Panadeine Forte) and oxycodone (e.g. Endone) and the most common benzodiazepines were diazepam (e.g. Valium) and temazepam (e.g. Normison)[iii].

Benzodiazepine Deaths

The Penington Institute Annual Overdose Report 2020[iv] details the increasing trend of drug induced deaths involving benzodiazepines since 2001. The annual deaths have increased by 45% since 2012. The Penington Institute has previously labelled benzodiazepines "Australia's silent killer", as they are the leading cause of all drug deaths.

The ABS states that in over 96% of drug-induced deaths where benzodiazepines were present, they were taken in conjunction with other drugs including [prescription opioids] and alcohol.[v] This information has also been submitted to the TGA from multiple sources including correspondence from state coroners. In 2016 the ABS's Director of Health and Vital Statistics, James Eynstone-Hinkins, said drug deaths were most commonly associated with benzodiazepines and oxycodone, noting that, "These are both prescription drugs which are used to manage anxiety and pain respectively".

Despite the estimated 10,000 deaths since 2001, the analysis I have provided shows that no benzodiazepine CMI since 2000 has ever contained any mention of the risk of death or the warnings that this could happen.[vi] The TGA's failure to provide these warnings to consumers in the CMI is well documented, including post your appointment to the TGA in 2012:

- The TGA was contacted about the escalating issues of addiction, abuse, and death due to benzodiazepines by the Victorian Coroners court in 2012. The coroner specifically discussed the "systemic public health issue" of co-prescribing benzodiazepines with opioids and the added risks of alcohol with these drugs[vii]. The TGA did not add these risks to the CMIs despite Professor Skerritt replying to the Coroner, advising that the Roche Valium February 2010 CMI[viii] contained the information for the safe and effective use of the medicine[ix]. However, the Valium CMI did not contain the risks as outlined by the coroner then, and 8 years later it still does not. The national death toll between 2001-2012 was **4,459**.
- In 2014 the TGA reviewed the scheduling of **all** benzodiazepines due to the increase in deaths from their use, notably when used with opioids. The TGA rescheduled Xanax and Alprazolam to Schedule 8 (Drugs of Addiction) due to the increased occurrence of addiction, death, and abuse[x] [xi]. Yet they did not update the CMI's to mention these risks, and 6 years later they still have not been updated. Today some Schedule 8 CMIs like the Genepharm Alprazolam CMI, have not been updated since July 2009[xii]! The risk of death was also not present in the Pfizer Xanax CMI[xiii], which Pfizer discontinued in 2013 when it was rescheduled to a Schedule 8 drug due to the deaths from its use. The national death toll between 2001-2014 was **5,749**.
- In 2016 the US Food and Drug Administration (FDA) added Boxed Warnings, to prescription opioid and benzodiazepine consumer warnings. This warning highlighted the risk of death when taken together "Taking benzodiazepines with opioid medicines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, breathing problems (respiratory depression), coma and death.[xiv]" The TGA made no changes to the CMIs for the same medications. In 2016 the national death toll in Australia was **7,260**.
- As with benzodiazepines, the opioid and codeine CMIs also contained no warning on the risk of death when they are combined, for over 20 years. However, in 2020 the TGA moved to improve several of the warnings in the opioid CMIs, including Endone and Panadeine Forte. An important addition is the warning statement that combining an opioid with benzodiazepines or alcohol can result in *"...in severe drowsiness, decreased awareness, breathing problems, coma and death."* Hence it defies belief that this warning was not also been added to the CMIs for benzodiazepine medications like Valium, especially considering

the loss of the life this warning could immediately prevent. The US FDA updated both the opioid and benzodiazepine consumer information in 2016, with these risks.

- In October 2020, the US FDA announced that benzodiazepines will be required to have an additional Boxed Warning added to the consumer medication information, due to the increasing problem of death, addiction, and abuse[xv]. This will highlight these risks to US consumers when reading the warning information, these are the same warnings that are not present in TGA regulated CMIs. There has been no comment on this from the TGA.
- In 2020, with the total deaths approaching **10,000**, Professor John Skerritt has on two occasions refused formal requests to review this mater and add these risks (including death) to the CMI.

Professor Skerritt, my questions to you are: How many deaths are required before the risk of death is included in the CMI? How many more lives need to be lost before the TGA acts on the warning failures in all benzodiazepine CMIs?

My reviews show that these side effects are represented in RACGP guidelines, TGA, and Dept Health resources. They are also present in US consumer warnings that are regulated by the US FDA, for the same medications made by the same companies. These risks are also present in the medication information that the pharmaceutical companies provide to health professionals (Product Information) but are then excluded from the CMI that they produce for the people taking the medication. The table below is explained in more detail in Appendix A.

Risks associated with Benzodiazepines					
	Aust Dept of Health	RACGP Guidelines	Product Information for GPs	Consumer Medicine Information (CMI)	US FDA Consumer Warnings
Death	✓	✓	✓	✗	✓
Coma	✓	✓	✓	✗	✓
Respiratory Depression	✓	✓	✓	✗	✓
Addiction	✓	✓	✗	✗	✓
Withdrawal Syndrome	✓	✓	✓	✗	✓
Abuse	✓	✓	✓	✗	✓
Increasing dependency risks	✓	✓	✓	✗	✗
Fatal risks during pregnancy	✓	✓	✓	✗	✓
Fatal risks with alcohol	✓	✓	✓	✗	✓
Fatal risks with antidepressants	✓	✓	✓	✗	✗
Fatal risks with codeine or opioid meds	✓	✓	✓	✗	✓
Fatal risk of an overdose	✓	✓	✓	✗	✓
Risk of suicidal thoughts	✓	✗	✓	✗	✓

Source: Prescribed Deaths 2020 www.prescribeddeaths.com.au See: Appendix A

Professor Skerritt, considering how well known the issues relating to benzodiazepines are, why has the TGA not ensured that these life-threatening risks and side effects are fully explained to consumers in the CMI?

When the TGA conducted scheduling reviews of benzodiazepines due to the increasing adverse harm and deaths, why was the CMI not updated to reflect the risks known to the TGA for Schedule 4 and 8 (Drugs of Addiction) benzodiazepines?

Why does the TGA have no approval process for the content of each CMI, especially the side effects, when that is the corresponding process the FDA follows in the US? How can the Australian Department of Health and the TGA endorse a document, which Australians trust to protect them from medication deaths, that has not been reviewed and formally approved by the TGA?

Why is it so important to have these risks contained in the CMI?

You have discussed the importance of the conversation with a patient and their doctor or pharmacist. A GP or pharmacist may verbally provide advice to a person on the medication; however, they rely on the CMI to reinforce and remind patients about this information. Confusion and difficulties concentrating are commons symptom of anxiety, insomnia, and panic attacks. Medication benzodiazepines are prescribed to treat.

The RACGP Benzodiazepine Guidelines state that benzodiazepines have especially been shown to impair vision, attention, information processing, memory, motor coordination and combined-skill tasks. Benzodiazepine CMIs list drowsiness, dizziness, light headedness, confusion, memory problems and sedation as side effects of taking the medication. The RACGP also state that a withdrawal symptom is poor memory and poor concentration.

This demonstrates that the people taking this medication, are almost certain to have some form of reduction in their ability to recall and process information. The CMI is the life-saving resource provided by the Department of Health to remind people of the information needed to prevent harm and death. If the CMI does not replicate the description of risks provided by a doctor or pharmacist (and the TGA), then it has failed in its responsibility to support this advice and to enable a patient to make an informed decision to take the medication. If the risks are not detailed, then they cannot be reinforced when a consumer reads the CMI at later times. The impact of the CMI not providing life-threatening side effect risks has legal implications that should not be easily dismissed.

This information is required in a written form to enable a provider, care giver or family member to be able to assist to safely administer the medication, or in the event of an emergency. The Department of Health advises that "Keep all your CMIs in the one place so you can easily find them. You may also need to re-check some details while using the medicine."[xvi] and "Always read the CMI before starting a new medicine. You may also want to refer to it while using the medicine — for example, to check if another medicine interacts with it, or what to do if you miss a dose." This would only be helpful if the CMI contained the information that it is legally required to contain.

TGA Responses

In my letter to you on the 4th August following your initial reply, I reiterated that I am not proposing that the PI and CMI be identical, only that the side effects are consistent between the two documents, as required by 'Schedule 12—Patient information documents' of the Therapeutic Goods Regulations 1990. The side effects that I have identified in PI (that are not in the CMI) like death, coma, addiction, withdrawal symptoms and abuse are easily understood and are not described in technical language. I have also pointed out that many of these side effects have been publicised in TGA consumer and industry updates, but they still are not in the CMIs.

I do agree the contents of the CMI should be framed in "*less technical language"*, but you have not provided any explanation why these side effects have not been included at all, in any part of the content. The CMI has a critical role in the Australian health care system, to explain side effects and that is what it must do, consistent with the PI. Understanding life-threatening risks in the PI may require a high degree of medical literacy, as it is written for health professionals, but the law requires they be explained in an easy to understand way in the CMI for consumers.

Australians may well have a "*low level of medical literacy*" but addressing that is the purpose of the CMI. Not including this information is not going to improve the knowledge of those taking the medication. These medications have widespread issues relating to addiction, abuse, and death. The challenge of reducing the incidence of these issues in the community would benefit from greater consumer awareness, which is the primary role of the CMI.

Medications dangerous enough to be classified as poisons, are prescribed without warning consumers why they are so dangerous. These medications are Scheduled 4 or 8 drugs due to the *exact* side effect risks that are not being disclosed in the CMI. The issue is not that the TGA is not aware of these risks, it is that they have refused to act to simply have them included the CMIs, to warn Australians and save lives.

COVID-19

Due to the increase in anxiety related mental health conditions during COVID-19, there are reports of an increase in benzodiazepine prescriptions by as much as 31%[xvii]. Based on PBS data, that would see the total number of prescriptions increase from 7 million to around 9 million a year. Potentially that could see the loss of life due to benzodiazepines increase by several hundred Australians, to around 1,200-1,300 each year.

No action was taken before COVID-19 on consumer awareness and the TGA has refused to act on the CMI warning failures that they are now aware of. My underlining message is that many of these deaths can be attributed to the lack of warning information in the CMIs and that without urgent changes to correct this the loss of life will continue, and potentially increase.

The Penington Institute also identifies the large number of deaths each year that are associated with prescription anti-depressants (e.g. Prozac) 591 deaths and anti-psychotics (e.g. Lithium) 318 deaths. The prescribing of these medications is reported to have increased by 22% and 46% respectively during COVID-19[xviii]. These medication classes are also represented in my research, with clear gaps in consumer warnings. I am concerned that more prescription medication deaths across a broad range of drugs could be an unintended consequence of COVID-19.

Professor Skerritt, your reply to Shane Rattenbury MLA did not accurately portrait the failings of the TGA regulated CMIs as I have detailed. The Department of Health advises Australians that the CMI is the reliable source for information on medication side effects for the *safe and effective use of prescription medicines*. However, you failed to disclose that the TGA has no process to review and approve the content of each CMI, that you ask Australians to trust. Any Minister for Mental Health or Health must be confident that CMIs reflect all the known risks and side effects based on current medial knowledge, especially those risks that impact mortality and morbidity of the population. They must also be confident that the regulator is regulating the warning documents. This is clearly not the case.

Restating my formal complaint

Professor Skerritt, opioids, benzodiazepines, codeine, antidepressants, antipsychotics, mood stabilisers and amphetamines are medications that have been prescribed to me since 2012. The risks that have not been included in the CMIs are risks that I have been exposed to, risks that have impacted my health and nearly cost me my life on two occasions. I have always been prescribed polydrug treatments – at least two and as many as seven medications at the same time. This complaint is not only about systemic issues that exist with medication safety, but also a complaint to the TGA about my personal adverse drug experiences with these medications.

I can assure you that my commitment to this complaint will continue until the TGA takes the required action. The issues examined in the report demonstrate that Australians like me will continue to be exposed to further adverse health events caused by systemic failures by the TGA to provide safe healthcare if action is not taken.

Regards

Patrick O'Connor Founder,

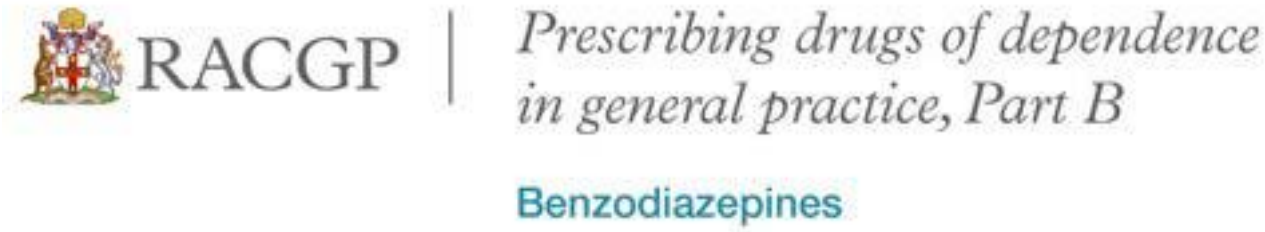
[redacted]

1st November 2020

CC: Shane Rattenbury

Appendix A:

The following are summaries of some of the serious risks not included in benzodiazepine CMIs.



"This guide is a resource to assist with the appropriate and accountable prescribing of benzodiazepines to prevent and reduce harms to patients, and to prevent medico-legal issues for GPs.", "GPs should be aware of the concerns associated with benzodiazepines such as potential dependence, withdrawal, problematic drug use (including diversion and misuse), and known harmful effects, including falls, potential cognitive decline and motor vehicle accidents. These risks should be discussed with patients."

1. Addiction

RACGP Benzodiazepine Guidelines - "In the 1980s, evidence of the addictive nature of benzodiazepines grew and it became generally accepted that benzodiazepines brought their own problems.", "…understanding of the risks and benefits of using potentially addictive drugs to manage your condition."

The Australian Government Department of Health warns that prescription addiction is a significant issue and that *many patients are unaware that prescription medications such as benzodiazepines like Valium, can be highly addictive*[xix] [xx]. They also warn that benzodiazepines should only be used for less than a month, and the shorter the safer, because they are addictive[xxi]. The reason why people are unaware of the risk of addiction is because it is not present in the benzodiazepine CMIs sourced from the TGA website. This is even though the TGA classes many benzodiazepines like Alprazolam (Xanax) as 'Drugs of Addiction'. As far back as 1991, Australia's top medical authority, the National Health and Medical Research Council, issued a warning that benzodiazepines should only be used for short periods as there was a high risk of addiction. No CMI has contained any warning of the risk of addiction since CMIs were introduced in 2000. No Schedule 8 benzodiazepine has mentioned the risk of addiction since they were classified 'Drugs of Addiction' in 2014.

2. Dependence

RACGP Benzodiazepine Guidelines - "Short-term therapy [1-4 weeks] is generally advised to reduce the risk of dependence and withdrawal, as well as other potential harm such as cognitive impairment.", "Benzodiazepine prescriptions [beyond 4 weeks] should be at the lowest effective dose and given intermittently, with regular reviews of the treatment plans and regular attempts at withdrawal.", "If dependence on benzodiazepines has become established, it is often difficult to treat and can become a long-term, distressing problem."

The CMI does warn that benzodiazepines should only be used for 2-4 weeks, that long term use is not recommended and that the use of benzodiazepines can lead to dependence on the medicine. The Valium information given to health professionals by Roche warns that *the risk of dependence increases with higher doses and longer use*[xxii]. However, this warning is not included in the CMI for

the consumers who take the medication. The Department of Health warns that dependence on pharmaceutical medicines can happen to anyone and often the person may not even be aware of it. This is an important warning as the RACGP Guidelines and international experts warn that benzodiazepine dependence can lead to *addiction and abuse*[xxiii]. Yet this additional risk of dependence is not included in the CMI. The Department of Health warns that dependence also means that if you stop taking the dose of medicine it can cause physical and mental *withdrawal symptoms*[xxivxxv].

The Royal Australian and New Zealand College of Psychiatrists released its updated *Guidance for the use of benzodiazepines in psychiatric practice*[xxvi] in 2019. It states "Patients should be advised that benzodiazepines may produce both tolerance and dependence, with the risk of withdrawal symptoms. Patients should also be informed of the full range of possible side effects, including cognitive impairment. Advice that the dosage and period of prescription are not to be exceeded should be clearly documented in the medical records. Patients should provide informed, formal consent when long term prescription of benzodiazepines is being considered and this should be documented in the notes."

3. Withdrawal Symptoms

RACGP Benzodiazepine Guidelines "There is evidence that some patients suffer protracted withdrawal symptoms that can continue for months to years after cessation", "..much higher incidences of withdrawal: in the order of 30–45% of patients who have used regular therapeutic doses of benzodiazepines for more than a few months.", "Up to 15% of patients who experience withdrawal will go on to have protracted symptoms lasting months to years."

The CMI mentions that your doctor may want you to gradually reduce the amount of the medication you are taking before stopping completely. This may help reduce the possibility of unwanted side effects. However, the CMI does not mention what these withdrawal symptoms actually are, the life-threatening nature of the risks or the long-term potential for the symptoms. Roche warn health professionals that after as little as one week of therapy, withdrawal symptoms can appear following the cessation of recommended doses. They also warn that withdrawal from Valium can take from 4 weeks to 4 months[xxvii].

The Department of Health states that benzodiazepine withdrawal symptoms that can last up to a year[xxviii], and the risks include seizures and death[xxix]. As far back as 1991, Australia's top medical authority, the National Health and Medical Research Council, issued a warning that benzodiazepines should only be used for short periods as there is a serious withdrawal syndrome after long-term use.

Table 4. Acute withdrawal symptoms

Anxiety symptoms		Distorted perceptions	Major incidents Mainly when high doses are stopped abruptly
Psychological	Physical		
• Anxiety • Panic attacks • Insomnia • Poor memory • Depression • Paranoia • Intrusive memories • Cravings • Nightmares • Excitability • Agoraphobia • Social phobia • Obsessions • Rage, aggression • Irritability	• Agitation • Tremor • Headache • Weakness • Dizziness • Nausea • Vomiting • Diarrhoea • Constipation • Palpitations • Rashes • Tingling, numbness, altered sensation • Fatigue • Flu-like symptoms	• Hypersensitivity to sound, light, touch, taste • Abnormal body sensation eg itching, pain, stiffness, blurred vision, paraesthesia, muscle twitching, tinnitus, burning sensations • Feeling self or world to be abnormal (depersonalisation or derealisation)	• Fits (1–2% of patients) • Delirium (rare) • Transient hallucinations (visual, tactile, auditory) or illusions (rare) • Psychosis (very rare)

Source: Prescribing drugs of dependence in general practice, Part B – Benzodiazepines.

4. Abuse

RACGP Benzodiazepine Guidelines "General practitioners (GPs) must consider multiple factors when prescribing benzodiazepines, including potential prescription abuse.", "[Diazepam has an] Increased risk for abuse because of quick onset."

Prescription medication abuse is the use of the drug other than as prescribed by a doctor, it generally occurs when a person becomes dependent or addicted to the drug. 1 million Australians misuse a pharmaceutical drug every year, with benzodiazepines the leading medications abused[xxx]. As with dependence and addiction, the risk of abuse for benzodiazepines is a reason why they are classed as controlled drugs by the TGA. The TGA states that benzodiazepines must be used with caution because of the risk of dependence and abuse, even when used at therapeutic doses for short periods[xxxi], yet this risk is not present in the CMIs.

5. Pregnancy

RACGP Benzodiazepine Guidelines "Benzodiazepines should not be prescribed, or prescribed with extreme caution, to women who are, or may be, pregnant.", "Benzodiazepines taken later in pregnancy (late third trimester), during labour or while breastfeeding are associated with risks to the foetus/neonate. They can cause neonatal drowsiness, respiratory depression, poor temperature regulation, poor feeding, hypotonicity ('floppy baby syndrome') and neonatal withdrawal syndrome."

According to Roche, the safety of Valium for use in human pregnancy has not been established. Use during pregnancy can cause premature birth or miscarriage, and the baby may suffer from respiratory depression, withdrawal syndrome, congenital malformation, or delayed development,.[xxxii][xxxiii] None of this information is contained in the Valium CMI.

6. Alcohol

RACGP Benzodiazepine Guidelines "When benzodiazepines are combined with other CNS depressants (eg alcohol, opioids), patients are at risk of respiratory depression, heavy sedation, coma and death.", "Alcohol and benzodiazepines can produce cross tolerance, and regular use of both can make withdrawal more severe and/or protracted."

Combining Valium with alcohol can cause severe sedation, respiratory depression, cardiovascular depression, coma, and death, according to Roche[xxxiv]. However, they only warn consumers in the CMI about the risk of drowsiness, confusion, dizziness and unsteadiness which may increase the risk of a fall. The risk of coma or death has never been included. On 23 March 1974 in The Canberra Times article titled, 'Drug and Drinking Danger', it was reported that Mrs Faye Dyson died, aged 41, from taking her Valium medication after drinking alcohol. Some 46 years, and thousands of deaths later, and the risk of death when combining Valium with alcohol is still not in the CMI.

Experts have also raised a warning that too many Australians are increasing their alcohol consumption due to mental health issues during COVID-19. A study by UNSW and the Black Dog Institute has shed light on the influence of COVID-19 on Australians' mental health.[xxxv] The researchers surveyed more than 5,000 people between 27 March and 7 April 2020 to explore people's anxiety levels and how they were coping over the outbreak.

A concern raised by the responses was the number of people reporting *excessive alcohol consumption as a way of dealing with their anxiety*. While 48.6 per cent of those with prior history of mental health diagnoses/problems reported excessive drinking, 54.6 per cent of people without prior mental health issues had also been drinking to excess.

7. Prescription Opioids and Antidepressants

RACGP Benzodiazepine Guidelines "Benzodiazepines present additional risk for someone being prescribed opioids in terms of overdose (fatal and non-fatal) and psychomotor impairment.", "It has been reported that the use of antidepressant drugs in combination with benzodiazepines may also increase the risk of overdose.."

In 2016 the ABS's Director of Health and Vital Statistics, James Eynstone-Hinkins, said drug deaths were most commonly associated with benzodiazepines and oxycodone, noting that, "These are both prescription drugs which are used to manage anxiety and pain respectively". ABS data shows that the combination of opioids (e.g. Endone) and benzodiazepines is one of the leading causes of drug deaths in Australia over the last decade[xxxvi]. The Endone CMI[xxxvii] warns that combining it with benzodiazepines can result in severe drowsiness, decreased awareness, breathing problems, coma and death. However, this warning is not included in the Valium CMI, in fact it has never even mentioned opioids or these risks, once in 20 years. The same issue exists for antidepressants, a medication commonly prescribed with Valium. The concurrent prescription of more than one benzodiazepine should generally be avoided and if necessary requires justification[xxxviii].

8. Overdose

RACGP Benzodiazepine Guidelines – "[Benzodiazepine] drug overdose, causing severe sedation and respiratory depression and death."

The Valium warning provided to health professionals in the PI details the side effects of respiratory depression, coma, and death. However, the Valium CMI describes an overdose as: If you take too much, you may feel drowsy, tired, confused, dizzy, have difficulty breathing, feel weak or become unconscious. There has never been any warning of the risk of coma or death in any benzodiazepine CMI ever produced.

9. Death

The risk of death is not mentioned once in any of the other benzodiazepine CMIs reviewed on the TGA website. The report also details the TGA's history of taking action on side effect issues, yet still failing to recognise that these side effects are not included in the CMIs. In 2014, the TGA rescheduled the benzodiazepine Alprazolam (Xanax) to a Schedule 8 drug due to the exponential increase in deaths associated with its use. The CMI contained no warning of the risk of *death* then, and six years later, it still doesn't. In fact the TGA allows CMIs for generic Xanax brands to be dispensed that have not been updated *since 2009*. It was also not present in the Pfizer Xanax CMI, which Pfizer discontinued in 2013 when it was rescheduled to a class 8 drug due to the deaths from its use.

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[ii] Australian Government, Department of Veterans' Affairs - Veterans Mates, Reducing the risk of falls, Sept 2017, see https://www.veteransmates.net.au/topic-48-therapeutic-brief

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[iv] Penington Institute, Australia's Annual Overdose Report 2020, Melbourne, 2020 see https://www.penington.org.au/wp-content/uploads/Australias-Annual-Overdose-Report-2020.pdf

[v] ABS 2017, Drug Induced Deaths in Australia: A changing story, see https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2016~Main%20Features~Drug%20Induced%20Deaths%20in%20Australia~6

[vi] *Prescribed Deaths*, O'Connor P, published 2020 see chapter two www.prescribeddeaths.com.au

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[viii] Roche Valium February 2010 CMI

[ix] Australian Government Department of Health Therapeutic Goods Administration, letter to Ms Kate Doherty, Subject: Investigation into the death of David A Trengrove, 6 November 2012. See https://www.coronerscourt.vic.gov.au/sites/default/files/2018-12/responsetga_trengrove.pdf
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[xxii] Roche Pharma, Valium Product Information, January 2020 see https://www.nps.org.au/medicine-finder/valium-tablets#full-pi
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