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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]

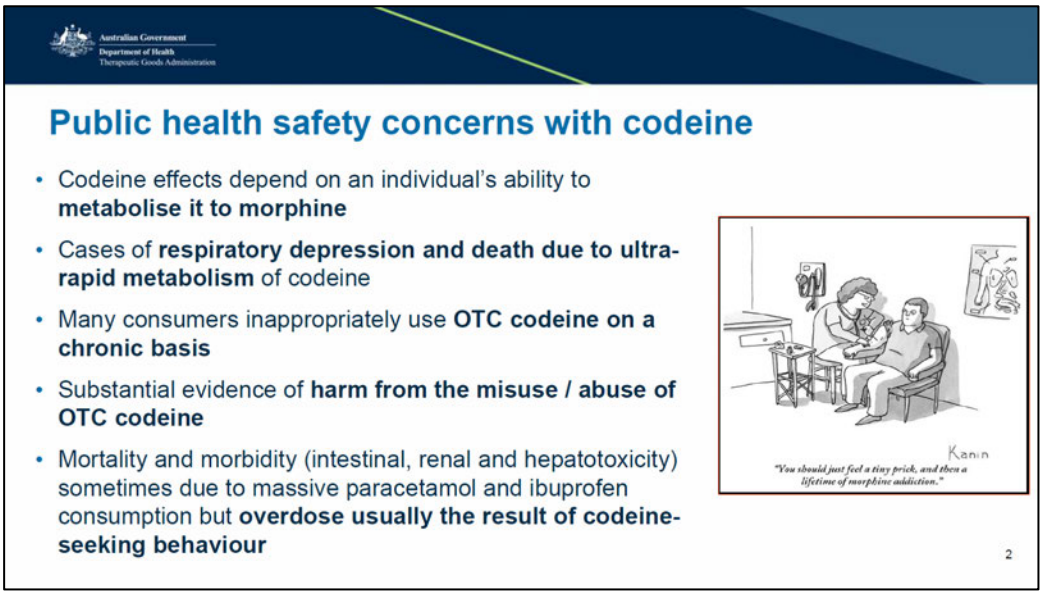
In the recording of the presentation, you discussed in detail the reasons for the changes, commenting:

> *"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
Founder, The Killing Zone
[redacted]

4 August 2020

CC: Commonwealth Ombudsman, [redacted]
CC: Royal Commission into Violence, Abuse, Neglect and Exploitation of People with Disability, [redacted]
CC: Royal Commission into Aged Care Quality and Safety, [redacted]

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.

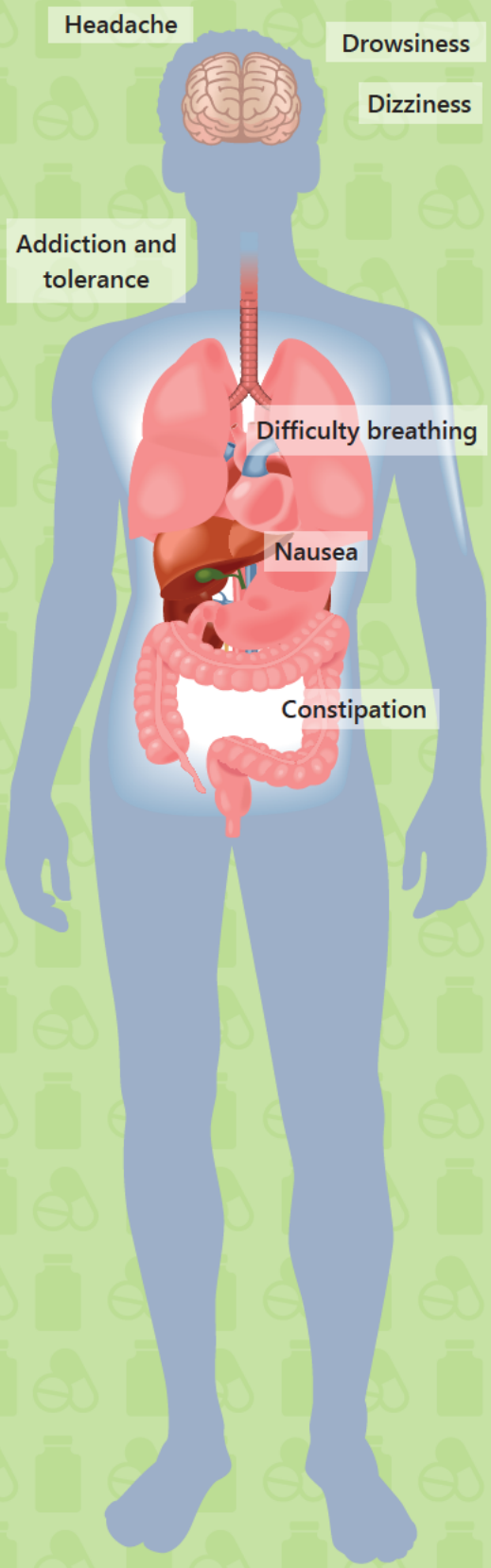
Codeine use can be harmful

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