Individual TGA Submission Prescription Opioid Use and Misuse in Australia., March 2018.

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I respectfully suggest both the Targin Product Information (PI) and the Targin Consumer Medication Information (CMI), require changes to update and strengthen the information provided, particularly in regard to dependence/addiction. These suggestions may also apply to other oxycodone or opioid medications.

Background and reasons for submission.

The area in which I work has the eighth highest rate of prescription opioid prescribing in Australia and I believe the highest in NSW. The majority of these PBS prescriptions, it is assumed, were written for the management of chronic pain.

One reason for this, apart from socio-economic factors, could be "…..*differences in access to alternative pain management options……".(1)*

An Addiction Medicine Specialist estimates 60% or more of the people he places on Opioid Substitution Treatment (OST), have developed their addictions/dependence, as a result of taking opioids prescribed for chronic pain.

Therapeutic Guidelines believes "*all patients taking long-term opioids will develop physical dependence" (6)*

A percentage of those people who became dependant, question why such an addictive substance was prescribed to them in the first place and may blame their prescriber; have they ignored the warnings or perhaps not been fully informed of the stigma and harm it may cause them in the future.

The CMI. (2)

a) The Targin CMI paragraph on dependence reads as follows: *As with all strong painkillers, your body may become used to you taking TARGIN tablets. Taking it may result in physical dependence. Physical dependence means that you may experience withdrawal symptoms if you stop taking TARGIN tablets suddenly, so it is important to take it exactly as directed by your doctor*. This paragraph does not give the complete definition of dependence (though I understand this definition is accepted by some), leaving out all reference to social or psychological dependence/addiction, although there is further mention of its abuse potential hidden away on page 4 of the CMI.

b) Those who are prescribed the opioids, are the ones who need the most information on the risks of addiction and its consequences, as well as the GP's.

   Therefore, I propose the much stronger information provided in the PI re dependence, should also be repeated in the CMI (with changes made to the first sentence; see PI below). This information needs to be in a prominent position on the first page of the CMI, under a heading such as **High Risk of Dependence and Addiction**
   This action may also help mitigate any feelings of anger or remorse, as in the situation described above, where addiction causes harm.

c) The CMI Side Effects states *"This means that the longer you take this medicine, the less it may cause problems for you*" This may be true for some minor side effects but patently untrue when Prescription Opioid Use Disorder is taken into account. There are also more serious side effects that need listing, including depression, anxiety, hormonal suppression and increased pain sensitivity.

d) Most importantly, the CMI needs to include the very real risk of accidental overdose and death, especially when taken with benzodiazepines. This risk needs to be highlighted on page1. Benzo's do not appear on the 'Taking other medications' list (as far as I can see).

e) At the bottom of the final page of the CMI, spaces could be assigned for signatures of the Prescriber and Recipient and perhaps the Recipients family as well. Theses signatures would attest to an awareness of all parties of the addiction risks involved in taking opioids.

f) A signed CMI, could then form part of a wider opioid agreement between patient and prescriber, with consideration being given to making an opioid "contract" mandatory for prescription doses above 60mg oMEDD.

The PI (3)

The Targin PI's paragraph on addiction risk states:

"Drug dependence

As with other opioids, tolerance and physical dependence tend to develop upon repeated administration of oxycodone. There is potential for abuse of the drug and for development of strong psychological dependence. TARGIN modified release tablets should therefore be prescribed and handled with a high degree of caution appropriate to the use of a drug with strong abuse potential. Like other opioids, TARGIN modified release tablets can be diverted for non-medical use, into illicit channels of distribution.

Withdrawal symptoms may occur following abrupt discontinuation of all oxycodone therapy including TARGIN modified release tablets. Therefore, patients on prolonged therapy should be withdrawn gradually from the drug if it is no longer required for pain control."

a) As mentioned, this paragraph could be copied into the CMI, to be read by the person who will take the Targin.

b) The first sentence could be rewritten:
"As with all opioids, tolerance with physical and psychological dependence, will develop over time or in as little as a week (5), after the first administration of oxycodone." (my words).

c) Page 10/32 of the PI, under Precautions states " *Hyperalgesia that will not respond to a further dose increase of oxycodone, may very rarely occur".*
This is wrong on two counts
there should be no encouragement to increase the dose if hyperalgesia is suspected.
It is not "rare". Saying it is uncommon but does occur in a significant number of people taking high dose oxycodone for long periods, is far closer to the truth.

MAX Doses

It's hard to justify the continuance of Targin 60mg and 80mg formulations (potentially 240mg oMEDD) for the treatment of CNCP on the basis of its approval as a second line option for Restless Leg Syndrome (RLS). No length of time is specified for its use, just a warning not to stop it.

My submission, in this instance, is to remove CNCP as an indication, for using these higher strength formulations; they may have a role in palliative care / cancer pain.

References

1) Safety and Quality-Opioids https://www.safetyandquality.gov.au/atlas/atlas-2015/atlas-2015-downloads/

2) CMI https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-CMI-04502-3&d=20180228161146224483

3) PI: http://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2012-PI-01399-3

4) Health Direct https://www.healthdirect.gov.au/medicines-and-addiction

5) CDC 3 days : https://www.cdc.gov/mmwr/volumes/66/wr/mm6610a1.htm

6) Therapeutic Guidelines https://tgldcdp.tg.org.au.acs.hcn.com.au/viewTopic?topicfile=chronic-pain-pharmacological-management&guidelineName=Analgesic#toc_d1e75

Terminology

Health Direct Australia, which is aimed at consumers, uses the terms **addiction** and **dependence** together in its headings. The distinction between the two terms differs between countries and specialties.

DSM V has chosen the neutral phrase Opioid Use Disorder (as part of a SUD), which in the context of chronic pain, can be narrowed to Prescription Opioid Use Disorder.

The AMA chooses SDBA - substance dependence and behavioural addictions.

In terms of the language to be used in the CMI, the word 'addiction', despite its connotations,would be understood by more consumers than 'dependence'; accepting that to be true, I would still use the word dependence along side it, as in High Risk of Addiction and Dependence, as Health Direct has done.