# Consultation: Non-steroidal anti-inflammatory drugs (diclofenac, flurbiprofen, ibuprofen, ketoprofen, mefenamic acid and naproxen) for oral use: proposed additional advisory statements for medicines

**4 February 2015**

**Closing date: 18 March 2015**



## Invitation to comment

The TGA is seeking comments from interested parties on the wording of proposed advisory statements for the non-steroidal anti-inflammatory drugs (NSAIDs) diclofenac, flurbiprofen, ibuprofen, ketoprofen, mefenamic acid and naproxen when included in non-prescription medicines for oral administration, which are proposed for inclusion in the Required Advisory Statements for Medicine Labels (RASML) document.

It is proposed that the new statements will be incorporated into the next update to RASML.

## Timetable

Document released for consultation on Wednesday 4 February 2015.

Interested parties should respond by close of business on Wednesday 18 March 2015.

Feedback will be released following consideration of submissions. (see 'What will happen').

## About the consultation

Recent TGA reviews and stakeholder feedback regarding cardiovascular safety of NSAIDs and safety of diclofenac have identified a need for additional RASML statements to the effect that excessive use of NSAIDs in medicines for oral use can increase the risk of heart attack and stoke; and that diclofenac can also increase the risk of liver damage.

With this consultation, the TGA is seeking comments on the proposed wording of these additional RASML advisory statements.

This consultation is intended to ensure that the label changes that are required for these medicines are made in the most convenient, efficient and cost-effective way.

## Background

### Scheduling of medicines

The Standard for Uniform Scheduling of Medicines and Poisons (SUSMP) sets out the level of control on the availability of medicines and poisons in Australia. The majority of medicines that are included in the SUSMP fall under one of the following classifications.

Schedule 2 - Pharmacy Medicine (available from a pharmacy without a prescription)

Schedule 3 - Pharmacist Only Medicine (available from a pharmacist without a prescription)

Schedule 4 - Prescription Only Medicine (available from a pharmacist with a prescription)

Medicines that are unscheduled or included in Schedule 2 or Schedule 3 of the SUSMP are collectively referred to as 'non-prescription' or 'over-the-counter' (OTC) medicines.

### Advisory statements on OTC medicine labels

The labels of OTC medicines contain information and directions for appropriate use, as well as any advisory statements (warnings) that are needed for safe and effective use of the medicines. Appropriate label advisory statements help ensure that consumers are able to self-select (where applicable) and use these medicines safely and effectively. Required advisory statements are compiled in the RASML[1].

From time to time the TGA becomes aware of the need for a new advisory statement(s) for a medicine or class of medicines. The need for a new advisory statement might arise from:

- The registration of a new medicine, a review of an existing medicine, or when new safety concerns for currently available medicines have been identified.
- A request from stakeholders and/or expert advisory committees.
- A change in the SUSMP scheduling that reduces the level of control and makes the medicine more widely available to consumers for self-selection or available without a prescription.

### Current RASML statements for non-steroidal anti-inflammatory drugs (NSAIDs)

The current edition of RASML (RASML No. 1) already requires oral OTC medicines containing any of the NSAIDs diclofenac, flurbiprofen, ibuprofen, ketoprofen, mefenamic acid or naproxen to carry on their labels the following advisory statements (with some small variations depending on the particular NSAID, and

whether it is intended for use in adults or children or for particular indications):

- Do not use [this product/ *insert name of product*] if you have a stomach ulcer
- Do not use [this product/ *insert name of product*] if you are allergic to [*insert drug name*] or other anti-inflammatory medicines
- If you get an allergic reaction, stop taking and see your doctor immediately
- Do not use [this product/ *insert name of product*] during the first 6 months of pregnancy except on doctor's advice. Do not use at all during the last 3 months of pregnancy.
- Unless a doctor has told you to, do not use [this product/ *insert name of product*] if you have asthma
- Unless advised by your doctor or pharmacist, do not use [this product/ *insert name of product*] with other products containing [*insert drug name*], aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly (*or alternative wording as set out in RASML No. 1*)
- Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful.

In addition, once the new RASML No. 2 comes into effect (on 12 December 2015) these medicines will also need to have the following additional statements:

- Do not use if you have impaired kidney function
- Do not use if you have heart failure.

### New RASML recommendations arising from the review of cardiovascular and hepatotoxicity safety of NSAIDs

In October 2014, the TGA published the outcomes of a review of the cardiovascular safety of NSAIDs, as well as a review of the safety of diclofenac. The reviews established that excessive or prolonged continuous use of oral NSAIDs increases the risk of heart attack or stroke. In addition, diclofenac also increases the risk of liver damage. These risks apply not only to consumers with known cardiovascular or hepatic disease or risk factors, but also to consumers who are otherwise healthy and without known risk factors.

In October 2014 the TGA also sought submissions from interested parties in regards to proposed actions arising from the safety reviews (this consultation closed on 6 November 2014).

A number of submissions were received from product sponsors and other organisations[2]. In regards to medicine labelling, the submissions were generally supportive of the need for additional cardiovascular safety statements (and hepatic safety statements for diclofenac) to be included on the labelling of existing products and incorporated into the RASML. However, before requiring amendments to labelling, the TGA should consult further with stakeholders on the precise wording to be used, and the TGA should allow an adequate transition period for the implementation of the changes.

[1]The RASML is registered on the Federal Register of Legislative Instruments (FRLI) as a legislative instrument titled Medicines Advisory Statements Specification 2014

[2]Those not marked confidential will be published on the TGA website in due course

## Proposal

The labels of oral medicines containing flurbiprofen, ibuprofen, ketoprofen, mefenamic acid or naproxen will

require an advisory statement to the effect that excessive or prolonged use can increase the risk of heart attack or stroke.

Similarly, an advisory statement to the effect that 'excessive or prolonged use can increase the risk of heart attack, stroke or liver damage' will be required on the labels of oral medicines containing diclofenac.

To minimise the total number of required statements for these medicine labels in the RASML, the TGA proposes that the new statements will be included in the RASML as extensions to the currently required statement 'Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful'; as follows.

For oral medicines containing flurbiprofen, ibuprofen, ketoprofen, mefenamic acid or naproxen:

- Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive or prolonged use can be harmful and increase the risk of heart attack or stroke.

For oral medicines containing diclofenac:

- Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive or prolonged use can be harmful and increase the risk of heart attack, stroke or liver damage.

It is proposed that these amended statements will be incorporated into the next update to RASML; and that there will be a transition period of 12 months from the date of publication of the updated RASML to allow sponsors time to amend their affected labels.

## Content of submissions

Submissions may address the proposed advisory statements and other identified issues. In addition, submissions might include:

- Whether or not you support the wording of the advisory statement. If you do not support the wording of the statement you may make suggestions for an alternative acceptable to you.
- An assessment of how the proposed change will impact on you. That is, what do you see as the likely benefits or costs to you (these may be financial or non-financial). If possible, please attempt to quantify these costs and benefits.

## How to respond

All submissions should be accompanied by a TGA submission cover sheet. Submissions must include full personal or organizational contact details (including address, telephone number and email).

Electronic submissions are preferred and should be emailed to rasml@tga.gov.au. Please include 'Consultation: Non-steroidal anti-inflammatory drugs (NSAIDs) for oral use - Proposed advisory statements for medicines' in the subject line of the email.

Alternatively, hard copy submissions may be mailed to:

RASML Officer
OTC Medicines Evaluation

Medicines Authorisation Branch
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

## What will happen

All submissions will be placed on the TGA Internet site unless marked confidential or indicated otherwise in the submission cover sheet (see Privacy information).

Submissions will be reviewed by the TGA and feedback on submissions will be provided through the TGA Internet site.

It is proposed that the advisory statements will then be included in the next update of the RASML.

## Privacy Information

The TGA collects your personal information in this submission in order to:

- contact you if the TGA wants to seek clarification of issues raised in your submission or to check whether you consent to certain information that you have provided being made publicly available.
- help provide context about your submission (e.g. to determine whether you are an individual or a director of a company or representing an interest group).

The TGA will disclose your name and (if applicable) your designation/work title on the TGA Internet site (i.e. make this information publicly available) if you consent to the publication of your name on the TGA Internet site (please complete the cover sheet).

Any text within the body of your submission that you want to remain confidential should be clearly marked 'IN CONFIDENCE'.

Please do not include personal information about other individuals in the body of your submission. Personal information in this context means information or an opinion about an individual whose identity is apparent, or can reasonably be ascertained, from the information or opinion.

## Enquiries

Enquiries should be directed via email to rasml@tga.gov.au

| Attachment | Size |
|---|---|
| Consultation submission: Non-steroidal anti-inflammatory drugs for oral use: proposed advisory statements for medicines (docx) | 61KB |

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