Australian Government
Department of Health
Therapeutic Goods Administration

Advisory Committee on Medicines

Meeting Statement

Meeting 1, Thursday 2 and Friday 3 February 2017

Role of the Advisory Committee on Medicines in the TGA's regulatory decision making process

The ACM is a statutory advisory committee established by the *Therapeutic Goods Regulations 1990*.

The TGA currently has seven statutory advisory committees from which it can obtain independent expert advice on specific scientific and technical matters to aid the TGA's regulatory decision making and other regulatory processes. The ACM provides advice to the TGA on, amongst other things, the safety, quality and efficacy of medicines, including in relation to pharmacovigilance.

The advice provided by the ACM is an important element in the undertaking of the regulatory functions of the TGA. However, it forms only part of the information that is available to a TGA delegate making a regulatory decision under the *Therapeutic Goods Act 1989*. While appropriate consideration will be given to such advice, it is important to note that neither a TGA delegate nor the TGA is obliged to seek this advice in making a decision or to follow it.

The purpose of this Meeting Statement is to describe in general terms the matters considered by the committee at each meeting and for it to be available as soon as reasonably practical after the relevant meeting.

Submissions for registration

The committee's advice was sought on nine applications for prescription medicines.

Update on the Australian Public Assessment Report (AusPAR)

An Australian Public Assessment Report (AusPAR) is compiled by the TGA after a delegate has made a decision relating to a submission for new prescription medicines and major changes to existing prescription medicines. It provides information about the evaluation of the submission and the considerations that led the TGA to approve or not approve the application.

The ACM (previously known as ACPM) was not advised of any updates with regards to AusPARs.

Pharmacovigilance

One pharmacovigilance item, on low dose methotrexate and dosing errors, was referred to the committee for its advice.

Methotrexate tablets are used to treat rheumatoid arthritis, severe psoriasis and some types of cancer. When methotrexate is used for the treatment of rheumatoid arthritis and psoriasis, it is typically prescribed in a once weekly dosage schedule. However, inadvertent dosing errors including accidental daily administration have led to serious toxicity and harm to patients.

Recently Cairns et al (Cairns R, Brown J, Lynch A, et al. A decade of Australian methotrexate dosing errors. MJA. 2016;204(10): 384e1-e6) summarised Australian adverse events associated with methotrexate dosing errors, referencing the TGA Database of Adverse Event Notifications (DAEN), the National Coronial Information System and data from Australian Poisons Information Centres and focusing on cases of accidental methotrexate daily dosing on at least three consecutive days.

Factors along the entire medicine management cycle can potentially contribute to inadvertent daily administration:

- Prescribing errors, including incorrect frequency on the prescription.
- Dispensing errors by pharmacists, including incorrect and unclear instructions, incorrect product selection, and incorrect packing of methotrexate into dose administration aids.
- Patient / carer error, including at the introduction of methotrexate as a new medicine, and confusion of methotrexate with other medicines (in particular, folic acid and prednisone).

Alerts published by international regulators and medicine safety organisations have recommended a multimodal approach to address methotrexate dosing errors, including:

- education for health professionals
- prominent alerts within prescribing and dispensing software
- promotion of careful patient counselling including the provision of suitable written material
- where possible, restriction of the quantity of methotrexate supplied to four weeks
- changes to packaging and labelling that promote once weekly dosing.

The ACM noted that some of these options may not be feasible or practical in the Australian context.

The ACM expressed concern that avoidable methotrexate dosing errors continue to cause significant harm to a small number of patients, mainly due to inadvertent daily ingestion, despite this being an identified risk for several decades.

The ACM advised that options to improve communications on the risk of dosing errors include:

- review wording and format of current warnings to simplify, reposition and emphasise critical safety messages in the Product Information (PI)
- prominently acknowledge the most common regimen is a single weekly dose of no more than 25 mg

- a separate 'black box' warning on dosing errors to appear on the first page of the PI
- reword the boxed warning in the dosage and administration section of the PI.

The ACM advised that additional risk management measures that could be considered by the TGA included:

- a patient dosing card
- reduced pack sizes to suit the contemporary clinical practice of weekly administration
- collaboration with education providers for health practitioner education
- warnings to be simple and as bold as possible.

The ACM advised that the product packaging could be redesigned to improve safe administration of methotrexate tablet. Options included:

- change the product name to include 'WEEKLY'
- require blister packaging, and printing of cautions and dosing instructions on the blister foil
- introduce 'Initiation'(smallest size) packs for patients newly prescribed methotrexate
- the message of 'TAKE ONCE WEEKLY unless otherwise directed' to be prominent on all packaging.

Risk Management Plans

A Risk Management Plan (RMP) is a set of pharmacovigilance activities and interventions designed to identify, characterise and manage risks relating to a medicine.

At this meeting, the RMP for a medicine with indications relating to psychiatric / psychological / behavioural disorders was referred to the committee for its advice.

The committee was asked to provide advice on matters including:

- the adequacy of the current consumer-directed risk minimisation measures for a specific risk
- whether further risk minimisation measures are warranted to improve communication to consumers of the specific risk, and if so, what measures should be considered.

Update on the publication of matters where the committee previously provided advice and a TGA decision has been made

This matter was not addressed for this inaugural committee meeting.

Further information

Meeting statements are made publicly available after each meeting.

For further information on the ACM, please visit Advisory Committee on Medicines

or contact the ACM Secretary by email ACM@health.gov.au.