Response to TGA Discussion Paper on Strengthening Monitoring of Medicines in Australia

Introduction

Thank you for the opportunity to comment on the TGA’s consultation on strengthening monitoring of medicines in Australia. We endorse the purpose behind this objective as stated in the discussion paper, i.e., “These enhancements are designed to proactively minimise, detect and address medicine safety-related issues.”

When drugs first appear on the market, there is limited knowledge about their safety. This is due to the limited number of people exposed to a drug in the pre-market period, the restricted inclusion criteria for clinical trials and to the relatively short period of time of these trials. Results from research in the United States (1) and Canada (2) have shown that about 1 in 5 drugs will eventually either acquire a serious safety warning or be completely removed from the market because of safety issues. Between 1990 and 2009, 4-5% of new drugs introduced onto the Canadian market in 5-year periods were withdrawn from sale because of safety problems (3). Moreover, up to 1 in 9 adult visits to emergency departments are due to drug-related adverse events (4). These visits are potentially preventable with resultant economic and health benefits.

The TGA discusses enhancements in four areas: adverse event reporting, compliance, improved collection and use of data and international information sharing and our response will deal with each of these areas.

Adverse event reporting

Enhanced data collection for adverse event reporting is necessary to better recognize adverse events. However, the ultimate objective is to use the information collected to improve understanding of a drug’s safety profile and to prevent similar adverse events from occurring in the future.

In formulating our recommendations about improving the detection of adverse drug events, we draw on evidence and experience largely from Canada. Canada was chosen as a comparator country for the purposes of this brief because the two countries possess a similar level of economic development, healthcare system, population size and limited resources for regulatory oversight compared with the United States or the European Union.

Because many adverse drug events are acute problems, they usually present to emergency departments. Emergency department patients presenting with an adverse drug event incur greater health services utilization and costs compared with patients presenting for other reasons (5). At present, healthcare practitioners working in emergency departments are not trained and do not have the time to be able to recognize the majority of these events (6) and as a result, patients may not receive the correct treatment. Failing to recognize adverse drug events leads to a number of potentially avoidable consequences:

1) patients may be re-exposed to the medications that caused their problem;
2) significant under-reporting of adverse drug events and therefore the actual benefit:harm ratio of medications will not be known;
3) if emergency physicians do not recognize drug-related visits then information from these events will not be included in subsequent outpatient adverse drug event surveillance programs that are intended to develop strategies to enhance drug safety (6).

There are a number of mutually non-exclusive options for enhancing recognition and reporting of adverse drug events. A study has been conducted in a tertiary care adult hospital in Vancouver, Canada where algorithms were used to identify patients potentially suffering from adverse drug events who presented to the emergency department. Pharmacists with clinical training then worked with physicians in the emergency department to evaluate these patients more intensively in order to determine if their problems were medication-related (4). Real time feedback mechanisms to clinicians results in a higher likelihood of reporting adverse drug events and allows them to modify the therapy that they are offering to their patients (7).

In Canada, consumers are the second most frequent source of adverse event reports to Health Canada (8). Patient reporting needs to be encouraged and systems put in place to allow this to happen.

**Recommendations to the TGA**

1. The TGA should advocate for better recognition of adverse drug events in emergency departments by recommending that hospitals place pharmacists with clinical training in that setting as was done in Vancouver and should provide support for this initiative by way of offering training programs in adverse event recognition and reporting. Such a system would complement what the TGA already has in place that currently receives adverse event reports from members of the public, general practitioners, nurses, other health professionals and the therapeutic goods industry.

2. The TGA should advocate for a system that makes reporting of adverse drug events by clinicians simple and quick to complete, and that supports clinical decisions at the point of care. Key factors for successful implementation are:
   a. the system itself,
   b. extensive involvement by clinicians (i.e., physicians, pharmacists and nurses), and
   c. the implementation process.

Platforms must be intuitive, user-friendly and easily accessible within electronic medical records, and must motivate documentation by making patient care safer. Patient- and medication-level data can then be integrated into administrative data, anonymized for surveillance and research purposes, and reported to external agencies, thus enabling the TGA to receive timely and representative data as a by-product of safer care.

3. Follow up information about adverse drug events that clinicians report should be sent back to them in a timely manner. This is already being done via letters in New Zealand (9) but we recommend electronic communication.

4. There is a need for patient education in two areas:
   a. to alert them as to what medications to be particularly concerned about, and
   b. to help them recognise when adverse drug events happen.

The current Black Triangle proposal from the TGA is one step in alerting patients about products whose safety is incompletely understood but in our view does not go far enough. Black Triangles should also be required on product labels or packaging, and all industry materials distributed to healthcare professionals that they are expected to pass on to patients, and for all promotional material directed at both healthcare professionals and
patients. Educational material should be based on the definition of an adverse drug event as “any untoward experience whether or not the event is thought to be drug related” (10). Patients should be intimately involved in designing the form that this education takes and its content to help ensure that they are user friendly in the multicultural context of Australian society.

5. There should be simple information sheets available for pharmacists and physicians to give out to patients with every prescription dispensed explaining how to report an adverse drug event. Patients and consumers should be intimately involved in the creation of these information sheets to help ensure that they are user friendly in the multicultural context of Australian society.

Compliance

The consultation paper from the TGA states that it “will implement a PV Inspection Program to enable TGA to proactively ensure companies have appropriate pharmacovigilance systems in place and are compliant with legal responsibilities.” We strongly support this measure and offer the following recommendations to complement what the TGA is already proposing.

Recommendations to the TGA

1. A time frame needs to be established for the publication of updates on the progress of confirmatory efficacy studies for provisionally registered medicines. This will allow for the collection of additional safety information in a timely manner.

2. All Periodic Safety Update Reports filed by manufacturers should be made public within 30 days of their receipt by the TGA.

3. The information about the results of the proposed Pharmacovigilance Inspection Program needs to be comprehensive including the names of the companies inspected, the deficiencies that were identified, corrective action that needs to be taken and the timeline for that corrective action to be completed. This information needs to be publicly reported on a regular basis.

4. There need to be meaningful sanctions put in place to ensure compliance by companies with the PV Inspection Program. We recommend a series of escalating sanctions whereby companies that repeatedly are not in compliance are subject to more severe penalties. The nature of these penalties should be the topic of further consultation by the TGA.

Improved collection and use of data

Improving the collection and use of data requires not only better methods of collecting the information about also the necessary resources to be able to analyse it and take the necessary steps to put those analyses into practice.

Recommendations to the TGA

1. The TGA should create a single national portal where patient-specific adverse drug events can be recorded and then accessed by clinicians across Australia. Having real time access to this data will help ensure that clinicians do not prescribe and dispense medications that are known to cause adverse drug events in particular patients. Appropriate privacy safeguards will have to be built into such a system but with an override in the case of an emergency.
2. The TGA should implement a system to generate safety signals for drugs at high-risk of causing adverse drug events. We recommend a Prescription Event Monitoring system, whereby all prescriptions for these drugs that are issued over a specified period of time are collected and the patients who received the prescriptions are tracked to look for any untoward events. The Drug Safety Research Unit in the United Kingdom conducts Prescription Event Monitoring. An electronic copy of targeted prescriptions, written by general practitioners and submitted to the Prescription Pricing Authority for claims reimbursement, is transmitted to the Drug Safety Research Unit. The Unit requests prescribers of target medicines to voluntarily complete a ‘green card form’ questionnaire for each patient detailing any adverse drug event(s), including deaths, following the prescription of newly marketed drugs (11, 12). This data is then analysed to look for unexpected adverse drug events or a higher frequency of adverse drug events than was initially anticipated.

3. Given the importance of linked prescribing and administrative health database as a tool to follow up the effects of drug treatments at a population level, we support the TGA’s intention to enhance data linkage. The aim should be to set up a national pharmacovigilance network similar to the Canadian Network for Observational Drug Effects studies (https://www.cnodes.ca/) which could be called upon to carry out investigations when TGA is faced with new signals of serious harm.

4. The TGA should consult regularly with an independent group of pharmacovigilance experts to discuss ways of continually enhancing its ability to proactively monitor postmarket drug safety.

5. The TGA should ensure that the number of full-time personnel and funding devoted to postmarket monitoring is equivalent to that devoted to reviewing new applications for drugs and biologics so that safety data can be properly analysed and acted upon.

6. The TGA should institute research to determine the effectiveness of its current methods for communicating safety issues to clinicians and consumers.

International information sharing

Harmonization, if done properly, could be beneficial nationally and internationally. However, harmonization must occur to standards that either maintain or improve national medication safety standards, ensure that marketed drugs offer significant therapeutic advances and preserve the scientific expertise within individual countries so that they can act independently when necessary.

Recommendations to the TGA

1. In the context of the information that the TGA receives from international sources, one of the fundamental requirements is that the TGA must be able to make that information public to be able to enhance the awareness of safety issues for the entire Australian community.

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References