MATTERS ARISING

Barriers in the quest for quality drug information: salutary lessons from TGA-approved sources for thyroid-related medications

A recent article drawing attention to the "inadequate, inaccurate or outdated" product information available for thyroid-related drugs prompted letters from several of our readers. ***(MJA 2007; 186: 76-79)***

Deficiencies in drug interaction information

Michelle Sweidan and James F Reeve

To the Editor: The National Prescribing Service recently reviewed drug interaction information in a range of prescribing and dispensing software systems and reference sources, including the Therapeutic Goods Administration (TGA)-approved product information (PI). Our findings support those of Stockigt[1] regarding the quality of information in PI.

An expert panel (see Acknowledgements) assessed 40 pairs of potentially interacting drugs (20 clinically important and 20 minor interactions) by examining the "Interactions" section of 80 PI monographs. The panel assessed both detection and content, using a range of parameters considered to be important in clinical decision making. For the clinically important drug interactions, these included useful management information (defined as sufficient information to proceed without looking elsewhere), pharmacological mechanism of interaction, clinical effects of the interaction, and time frame (onset, duration).

For clinically important interactions, 38 of 40 PI monographs listed the potential interaction; however, there were considerable shortcomings in the amount and quality of information provided. Only five of 38 monographs (13%) provided useful information about management. The mechanism was described in 15 monographs (39%) and clinical effects in 19 (50%); time frame was mentioned in only one (3%). In addition, there were many inconsistencies between any two monographs for a particular drug pair — not surprising given that the information is usually developed by different drug manufacturers at different times.

The results of our study suggest that in many cases the PI for a drug does not provide useful information about potential drug interactions. For decision support to be useful to health practitioners, information must be sufficiently detailed and relevant. Poor quality, irrelevant or inconsistent information is at best unhelpful or a waste of time, and at worst may prompt an inappropriate management decision, potentially compromising patient care. While epidemiological evidence for drug interactions is limited, good quality information and practical advice is available in a number of specialised drug interactions reference sources. This issue will be discussed in more detail with the full results of our study, which will be submitted for publication later this year.

Acknowledgements: We worked with an expert panel on this project: Professor Jo-anne Brien (Clinical and Academic Pharmacist), Dr Pradeep Jayasuriya (General Practitioner), Dr Jennifer Martin (Physician and Clinical Pharmacologist), and Mr Graeme Vernon (Drug Information Pharmacist).

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1 Stockigt JR. Barriers in the quest for quality drug information: salutary lessons from TGA-approved sources for thyroid-related medications. *Med J Aust* 2007; 186: 76-79. ❑

Specialist societies can assist

Leon A Bach

To the Editor: On behalf of the Endocrine Society of Australia, I would like to endorse the views expressed by Stockigt that the Therapeutic Goods Administration (TGA)-approved information sources for thyroid-related medications are outdated.[1] His examples are compelling evidence that statements within product information (PI) sources are inconsistent with current practice. The consequences of these statements range from confusing to potentially dangerous.

The current process for updating PI appears to exclude expert advice from specialist practitioners who are most likely to be aware of recent developments regarding the use of medications specific to their practice. In most areas of medicine, specialist societies representing these practitioners provide an excellent potential "first port of call" for the TGA and suppliers to source expert, evidence-based assistance in updating PI. Certainly, the Endocrine Society of Australia is willing to act in this capacity for endocrine-related drugs, and I would be very surprised if this were not the case for other specialist societies.

In summary, a partnership between all parties involved in the provision of quality care is needed to ensure that PI is contemporary and accurate.

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1 Stockigt JR. Barriers in the quest for quality drug information: salutary lessons from TGA-approved sources for thyroid-related medications. *Med J Aust* 2007; 186: 76-79. ❑

Misleading information for consumers

David Torpy

To the Editor: I concur with Professor Stockigt's recent article[1] outlining the shortcomings of product information (PI) for thyroid-related drugs. I often need to contradict incorrect or even hazardous PI advice given to patients.

An example is the consumer medicine information (CMI) available on the MIMS website, the "myDr" service.[2] Although Hysone (hydrocortisone, Alphapharm) is often used for cortisol replacement, rather than as anti-inflammatory therapy, much of the CMI makes no distinction between these two uses. This may, in part, underlie the potentially dangerous advice: "Do not take Hysone if you have any infections that are not being treated or are not responding to treatment".[2] This instruction implies that patients should stop taking Hysone when they have an infection; this may be disastrous for those with adrenal insufficiency because it could lead to an adrenal crisis.[3] It is necessary to *increase* replacement dosages in the event of an infection, intercurrent illness or surgery.[3]

The CMI for Cortate (cortisone acetate, Aspen Pharmacare), the alternative glucocorticoid replacement drug, has similar information: "Do not take CORTATE if you have an uncontrolled infection".[4]

In the editorial accompanying Stockigt's article,[5] Dowden acknowledges that PI needs to be kept up to date, but I think that PI and CMI will remain inadequate without expert professional review, in addition to that currently mandated by the Therapeutic Goods Administration.

Patients with adrenal insufficiency need reliable information about the replacement medications they take long term. The CMI for these

two drugs is in need of urgent revision in the interests of patient safety.

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1 Stockigt JR. Barriers in the quest for quality drug information: salutary lessons from TGA-approved sources for thyroid-related medications. *Med J Aust* 2007; 186: 76-79.
2 MIMS. myDr.com.au. Consumer medicine information. Hysone. http://www.mydr.com.au/drugs/cmi.asp?cmicode=2098&prodcode=068201 (accessed Mar 2007).
3 Stewart PM. The adrenal cortex. In: Reed Larsen P, Kronenberg HM, Melmed S, Polonsky KS, editors. Williams textbook of endocrinology. 10th ed. WB Saunders, 2003: 531-532.
4 MIMS. myDr.com.au. Consumer medicine information. Cortate. http://www.mydr.com.au/drugs/cmi.asp?cmicode=2496&prodcode=067201 (accessed Mar 2007).
5 Dowden JS. Product information past perfect [editorial]. *Med J Aust* 2007; 186: 51-52. ❑

MIMS is not a stand-alone resource

Elizabeth A Donohoo

To the Editor: The discussion regarding increased currency and updating of prescription drug information (product information, PI)[1] provides on opportunity for insightful and valuable debate. MIMS (a compilation of PI)[2] supports any initiatives that result in PI and consumer medicine information (CMI) being updated more regularly, and I would like to clarify MIMS' specific role in the process.

PI is an invaluable information source, but not the only source. Accordingly, MIMS was never intended to be used as a stand-alone resource, without appropriate clinical experience and reference to other resources, where warranted. Although this was not mentioned in Stockigt's article,[1] it is clearly stated on the Foreword page of *MIMS annual*.[2]

Stockigt, in various comments he made to the media, observed that his article reviewed only one class of drugs[1] — thyroid medication — which has been notable for its lack of new products or information in recent years. Thus, his findings cannot be extrapolated across the entire pharmaceutical database. Dowden's editorial,[3] however, appears to suggest that outdated PI is common. This is an assertion with which MIMS must strongly disagree.

One measure of the currency of a medicine information database is the frequency and number of updates. MIMS currently publishes more than 100 changes to PI every month, and has the processes and people in place to make an even greater number of changes more frequently should this information become available. However, ultimately the responsibility for updating PI lies with the pharmaceutical industry, and all changes must be approved by the Therapeutic Goods Administration; only then can PI be disseminated by MIMS.

MIMS believes that PI, while a valuable resource, is not a stand-alone resource. This is supported by the fact that the entire range of MIMS electronic decision-support modules, such as MIMS DrugAlert (drug–drug interactions) and MIMS AllergyAlert (drug–allergy warnings), are, in fact, derived from reviews of the primary international literature. MIMS welcomes the opportunity to discuss this perspective.

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1 Stockigt JR. Barriers in the quest for quality drug information: salutary lessons from TGA-approved sources for thyroid-related medications. *Med J Aust* 2007; 186: 76-79.
2 MIMS annual. 30th ed. Sydney: CMPMedica Australia, 2006.
3 Dowden JS. Product information past perfect [editorial]. *Med J Aust* 2007; 186: 51-52. ❑

The National Prescribing Service should lead

Jim R Stockigt

In reply: It is encouraging that Donohoo, on behalf of MIMS, supports initiatives to more regularly update product information (PI). My review[1] demonstrates that necessity. The material published by MIMS is apparently not under their direct editorial control; it depends on PI from the pharmaceutical industry, vetted by the Therapeutic Goods Administration. Revision of PI by drug sponsors has major inertia.[2]

While the problems in the thyroid area can be serious for a fraction, perhaps 1%–2% per year, of the 200 000 people who take thyroid medications, I made no assertion that the deficiencies identified for thyroid-related medications reflect other PI-based information; that question remains open.

Donohoo emphasises that the PI-based information in MIMS is not a stand-alone resource for health professionals, who are able to choose between sources of drug information. By contrast, consumers are offered PI-based consumer medicine information (CMI) as a definitive resource, without choice. The obligatory link between PI and CMI[3] is a compelling reason for revision of PI.

In my view, the National Prescribing Service, an organisation that publishes the journal *Australian Prescriber* and fosters quality use of medicines, is the national resource best placed to show initiative to improve the current deplorable state of thyroid-related PI which is, in my view, an impediment to safe, well informed health care for some thousands of Australians. Together with Donohoo, I support debate and initiative.

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1 Stockigt JR. Barriers in the quest for quality drug information: salutary lessons from TGA-approved sources for thyroid-related medications. *Med J Aust* 2007; 186: 76-79.
2 Dowden JS. Product information past perfect [editorial]. *Med J Aust* 2007; 186: 51-52.
3 Therapeutic Goods Administration. Initial discussion paper: improving access to prescription medicines information. Apr 2005. http://www.tga.gov.au/consult/2005/accesspmi.pdf (access Mar 2007). ❑

Call in independent information sources

John S Dowden

In reply: The publications reviewed in Stockigt's article[1] are compendia of product information (PI). Their currency therefore relies on manufacturers keeping the PI up to date. A short scan quickly shows that the PI of some brands has apparently not needed amending for more than 5 years. Examples include certain brands of digoxin (last updated in 2000), roxithromycin (2000), levamisole (1999), levocabastine (1998), pindolol (1993) and ergometrine (1991).

Many monthly changes to PI may be made, but, as stated in my editorial,[2] it is not always clear whether these changes are substantial amendments or minor variations. To assess whether PI reflects current practice would require Stockigt's research to be replicated with other drug classes.

As PI is brand-specific, the amount of comparative information it contains is limited. This is where information sources independent of the pharmaceutical industry, such as the *Australian medicines handbook* (http://www.amh.net.au/), *Therapeutic guidelines* (http://www.tg.com.au/), and the National Prescribing Service (http://www.nps.org.au/) can assist.

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1 Stockigt JR. Barriers in the quest for quality drug information: salutary lessons from TGA-approved sources for thyroid-related medications. *Med J Aust* 2007; 186: 76-79.
2 Dowden JS. Product information past perfect [editorial]. *Med J Aust* 2007; 186: 51-52. ❑

Medicines and breastfeeding: information is available on safe use

Lisa H Amir

To the Editor: In his review of drug information for thyroid-related medications, Stockigt noted the "outdated advice that antithyroid drugs are not compatible with breastfeeding."[1] However, outdated product information is not unique to antithyroid drugs. Product information rarely states that the drug is safe or advisable for breastfeeding women.

Many women receive medicines in the postpartum period: a UK study found that 54% of women were given a drug in hospital and 55% were given a prescription by their general practitioner.[2] Yet many breastfeeding women who need medicines are being given incorrect advice, as illustrated by the experience of my podiatrist, Janet.

Breastfeeding was going well when, at 4 months postpartum, Janet fell down a flight of stairs. Neither the ambulance officers nor the metropolitan emergency department registrar were willing to administer any pain relief except paracetamol ("unless you are prepared to wean") — although Janet was in excruciating pain with a fractured 12th rib. At 7 months postpartum, Janet was hypertensive despite treatment. Regardless of her strong desire to continue breastfeeding, her GP and specialist informed her that she needed to change medication and therefore would have to stop breastfeeding.

Janet's case illustrates two issues: firstly, a breastfeeding woman was denied necessary medication because she was breastfeeding, and secondly, her infant was denied continued breastfeeding because of maternal medication. Apparently none of the health professionals sought expert help with decision making surrounding medicines and breastfeeding. Janet encouraged me to use her story to educate other health professionals.

For the vast majority of maternal medications, the amount of medication an infant would receive through breastfeeding is less than 1% of an infant dose. In general, if the medication is safe to use in infants, it will be safe for the breastfeeding mother. Only a small number of medications are contraindicated during breastfeeding: these include antineoplastic agents, ergotamine, methotrexate, cyclosporin, and radiopharmaceuticals.[3]

Information is available about safe use of medicines while breastfeeding (Box). The sources listed in the Box have reviewed the available evidence on individual drugs and given recommendations on whether they are safe to use during lactation. In general terms, they have followed the recommendations for evaluating appropriateness of off-label medicines as suggested by a recent New South Wales working party.[4] Medicines used during *pregnancy* are given safety ratings and the information is available online.[5] Australian clinicians need to access such guidance in relation to safe prescribing for *breastfeeding women*.

Sources of information on medicines for breastfeeding women

Reference books

Pharmacy Department, Royal Women's Hospital, Melbourne. Drugs and breastfeeding. Melbourne: RWH, 2004 (available for sale: tel: 03 9344 2484)

Hale TW. Medications and mothers' milk. 12th ed. Amarillo, Tex: Pharmasoft Medical Publishing, 2006 (available for sale at: http://neonatal.ttuhsc.edu/lact)

Websites

Drugs and lactation database (LactMed), a new searchable website set up by the US National Library of Medicine (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT)

World Health Organization. Breastfeeding and maternal medication (http://www.who.int/child-adolescent-health/New_Publications/NUTRITION/BF_Maternal_Medication.pdf)

Telephone advice

Pharmacy departments of tertiary maternity hospitals

Drug Information Centre, Pharmacy Department, Royal Women's Hospital, Melbourne (tel: 03 9344 2277) ◆

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1 Stockigt JR. Barriers in the quest for quality drug information: salutary lessons from TGA-approved sources for thyroid-related medications. *Med J Aust* 2007; 186: 76-79.

2 Jones W, Brown D. The medication vs breastfeeding dilemma. *Br J Midwifery* 2003; 11: 550-555.

3 American Academy of Pediatrics Committee on Drugs. Transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; 108: 776-789.

4 Gazarian M, Kelly M, McPhee JR, et al. Off-label use of medicines: consensus recommendations for evaluating appropriateness. *Med J Aust* 2006; 185: 544-548.

5 Therapeutic Goods Administration Australian Drug Evaluation Committee. Prescribing medicines in pregnancy. An Australian categorisation of risk of drug use in pregnancy. 4th ed. Canberra: Commonwealth Department of Health and Aged Care, 1999.