MADRAC

Malaysian Adverse Drug Reactions Newsletter

National Pharmaceutical Control Bureau,
Ministry of Health Malaysia

This newsletter is also available on our website: http://www.bpfk.gov.my

To report an adverse drug reaction:

1. Visit http://www.bpfk.gov.my,
2. Click on "MADRAC (Adverse Drug Reactions)" on the left toolbar; and
3. Click on "Reporting Online".

Alternatively, please contact:

National Centre for Adverse Drug Reactions Monitoring,
Centre for Post Registration
National Pharmaceutical Control Bureau
Ministry of Health
P.O. Box 319, 46730 Petaling Jaya, Selangor, Malaysia

Tel : +603 7883 5400
Fax : +603 7956 7151

Contents

- SAFETY ISSUES OF CURRENT INTEREST
  - Champix® (Varenicline)
  - Mycophenolate Mofetil (Cellcept®) and Mycophenolic Acid (Myfortic®) – Risk in Pregnancy
  - Cefepime – Reports of Death
  - Cellcept® (Mycophenolate Mofetil) and Myfortic® (Mycophenolate Acid) and the Development of Progressive Multifocal Leukoencephalopathy
  - Use of Cough and Cold Products in Children Under Two Years Old – An Update
  - Exubera® (Recombinant Human Insulin) and Primary Lung Malignancy
- REGULATORY MATTERS
  - Incidence of Myocardial Infarction in Pregnant Women Receiving Beta Agonist to delay Pre – Mature Labour – Additional Warning and Precaution
  - Low Molecular Weight Heparin – Clexane® Prefilled Syringes (Enoxaparin)
  - Cardiamed® - An Update
- LOCAL CASE REPORTS
  - Drug Exposure During Pregnancy – Olanzapine
  - Kisan® Injection 10mg/ml
  - A Reminder: Metoclopramide – Usage in Children

Issued:

SAFETY ISSUES OF CURRENT INTEREST

CHAMPIX® (VARENICLINE)

Champix® is a Group C medicine indicated for smoking cessation in adults. It is available in Malaysia in two strengths; 0.5mg and 1.0mg.

The European Committee for Medicinal Products for Human Use (CHMP) has been closely monitoring the safety of Champix® since it was first registered in the European Union (EU) in September 2006. It was found that depression has been reported in patients who were trying to stop smoking using Champix®. Symptoms associated with depression were suicidal ideation and suicide attempt.

Hence, in December 2007, the CHMP requested the registration holder, Pfizer, to update the product information for Champix® in order to inform doctors and patients of the occurrence of depression in patients trying to stop smoking with Champix®.

This warning is included in Malaysia's prescribing information leaflet under sections "Special Warnings and Precautions for Use" and "Undesirable Effects". However, this information is not clearly stated. The Drug Control Authority (DCA) is in the midst of a discussion with Pfizer to ensure that this information is clearly seen in the product information leaflet. Meanwhile a letter has been sent to the Malaysian Medical Association and the Malaysian Pharmaceutical Society to disseminate this information and to request their assistance to alert their members of this safety concern.

Reference:

1. European Medicines Agency (EMEA), European Medicines Agency concludes new advice to doctors and patients for Champix needed. Media Release : 14 Dec 2007, http://www.emea.europa.eu

MYCOPHENOLATE MOFETIL (CELLCEPT®) AND MYCOPHENOLIC ACID (MYFORTIC®) – RISK IN PREGNANCY

The United States Food and Drug Administration (USFDA) received reports of infants born with serious congenital anomalies, including microtia and cleft lip and palate, following exposure to mycophenolate mofetil (MMF) during pregnancy. MMF is an ester of the active metabolite mycophenolic acid (MPA). In most of the cases, MMF was indicated following an organ transplant that the mothers had to prevent organ rejection. In some of the other cases, MMF was indicated for immune – mediated conditions such as systemic lupus erythematosus (SLE) and erythema multiforme. The mothers were taking MMF before they were pregnant until the first trimester or until the pregnancy was detected.

MMF and MPA also increase the risk of spontaneous abortion in the first trimester and can cause congenital malformations in the infants of women who are treated during pregnancy. The USFDA has revised the labeling for both MMF and MPA in November 2007 to change the Pregnancy Category to "D" i.e. positive evidence of human fetal risk, but potential benefits may warrant use of the drug in pregnant women

despite the potential risk. These findings about risk of early pregnancy loss and congenital malformations were also added to the boxed warning.

In Malaysia, Roche (Cellcept®) and Novartis (Myfortic®) have been instructed to update the labeling for their products as per USFDA's recommendations and issue a Dear Healthcare Professional Letter to inform all health professionals of these labeling changes.

Reference:

1. Medwatch, U.S.F.D.A http://www.fda.gov/cder/drug/InfoSheets/HCP/mycophelolateHCP.htm

CELLCEPT® (MYCOPHENOLATE MOFETIL) AND MYFORTIC® (MYCOPHENOLATE ACID) AND THE DEVELOPMENT OF PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

The USFDA is investigating the potential association between the use of Cellcept® and Myfortic® and the development of Progressive Multifocal Leukoencephalopathy (PML). PML is a rare, life threatening disease which affects the central nervous system. It usually occurs in patients with suppressed immune systems (by disease or medicines).

The USFDA is currently reviewing post – marketing reports of PML in patients who took Cellcept® or Myfortic® and data submitted by Roche. The USFDA also requested data on PML cases for Myfortic® from Novartis. Novartis was also requested to revise the Myfortic® prescribing information to include information about PML that has been included in the Cellcept® prescribing information.

Meanwhile, the USFDA advised patients and healthcare professionals to be aware of the possibility of PML, usually in the form of loacalized neurologic signs and symptoms in the setting of a suppressed immune system, including during therapy with Cellcept® and Myfortic®.

In Malaysia, the DCA has instructed the registration holders, Roche and Novartis to communicate the conclusions and recommendations to us once the review is completed.

Reference:

1. Medwatch, U.S.F.D.A, http://www.fda.gov/medwatch/safety/2008/safety08.htm#mycophenolate

CEFEPIME – REPORTS OF DEATH

The USFDA has issued an early communication to inform the public of an issue the Lancet Infectious Diseases has raised. The Lancet Infectious Diseases queried the increase in mortalities with the use of cefepime, a broad spectrum β-lactam antibiotic. **It was described that the all-cause mortality was higher with cefepime as compared to other β-lactam antibiotics and for the subgroup of patients with febrile neutropenia in the meta-analysis.**

The USFDA together with Bristol-Myers Squibb will be further evaluating the finding of increased mortality in patients who received cefepime. The evaluation will take a few months to complete and USFDA will announce its conclusions and recommendations, if any, to the public. Meanwhile, healthcare professionals are advised to be aware of the risks and benefits described in the prescribing information and the new information from this meta-analysis when considering the use of cefepime.

In Malaysia, cefepime is marketed as Maxipime® and Megapime®. It is indicated in adults for

- Lower respiratory tract infections, including pneumonia and bronchitis
- Urinary tract infections, both complicated, including pyelonephritis, and uncomplicated infections
- Skin and skin structure infections
- Intra-abdominal infections, including peritonitis and biliary tract infections

- Gynecologic infections
- Septicemia
- Empiric treatment in febrile neutropenia

It is also indicated in pediatrics for

- Pneumonia
- Urinary tract infections, both complicated, including pyelonephritis, and uncomplicated
- Skin and skin structure infections
- Septicemia
- Empiric treatment in febrile neutropenia

The Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) will continue to monitor this issue and the safety information will be disseminated to all healthcare professionals once the evaluation is completed.

References:

1. WHO Pharmaceuticals Newsletter No. 5, 2007, Pg. 4, “Cefepime: Reports of death being investigated”.
2. Medwatch, U.S.F.D.A., http://www.fda.gov/cder/drug/early_comm/cefepime.htm

USE OF COUGH AND COLD PRODUCTS IN CHILDREN UNDER TWO YEARS OLD – AN UPDATE

The Australian Therapeutic Goods Administration (TGA) has informed all pharmacists and medical practitioners that cough and cold products containing sedating antihistamines will only be available as prescription medicines in children under the age of 2 years.

In February 2008, the National Drugs and Poisons Scheduling Committee reviewed these cough and cold medicines at its meeting and concluded that the risks of using these drugs as over-the-counter preparations outweigh the benefit. Adverse drug reactions (ADRs) such as agitation, hallucinations, insomnia and over sedation have been reported.

From 1 September 2008 onwards, these medicines will not be available to children under the age of 2 years without a prescription from a medical professional. The TGA has informed all registration holders of cough and cold medicines for children to stop labeling these products as suitable for children under the age of 2 years.

In Malaysia, medical professionals have been advised to weigh the risks and benefits before prescribing cough and cold products to children less than 2 years old. Currently, no labeling changes were instructed by the DCA for the cough and cold products. However, on the 21 February 2008, an advisory letter on this issue was circulated to the Pharmaceutical Services Division Ministry of Health, Academy of Medicine, Malaysian Medical Association, Association of Private Hospital Malaysia and Malaysian Pharmaceutical Society to disseminate this information to all healthcare professionals.

Meanwhile, the Canadian and United States Drug Regulatory Agencies will be reviewing the safety of such products for children between the ages of 2 to 11 years old. The DCA will evaluate the results of these reviews once they are completed to assess any need for labeling changes.

Reference:

1. Reactions Weekly, Uppsala Monitoring Centre, “Cough and Cold Medicines Prescription Only for Under Twos”, 19 Apr 2008, No. 1198.

EXUBERA® (Recombinant Human Insulin) AND PRIMARY LUNG MALIGNANCY

Pfizer in the United States has informed healthcare professionals and patients of the **6 newly diagnosed cases of primary lung malignancies in clinical trials among Exubera® – treated patients** and 1 newly diagnosed case among comparator treated patients. It was also reported that there was 1 post – marketing report of a primary lung malignancy in an Exubera® – treated patient. However, all the patients who were diagnosed with lung cancer had a prior history of cigarette smoking. Besides that, there were too few cases to determine whether there is an association between Exubera® and primary lung malignancy.

However, Pfizer has updated Exubera®'s prescribing information at the WARNINGS section to include:

In clinical trials of Exubera, there have been 6 newly diagnosed cases of primary lung malignancies among the Exubera – treated patients, and 1 newly diagnosed case among comparator treated patients. There has also been 1 post – marketing report of a primary lung malignancy in an Exubera – treated patient. In controlled clinical trials of Exubera, the incidence of new primary lung cancer per 100 patient – years of study drug exposure was 0.13 (5 cases over 3900 patient – years) for Exubera – treated patients and 0.02 (1 case over 4100 patient – years) for comparator – treated patients. There were too few cases to determine whether the emergence of these events is related to Exubera. All patients who were diagnosed with lung cancer had a prior history of cigarette smoking.

Exubera® is registered in Malaysia in two strengths; 1 mg and 3 mg. The DCA has requested Pfizer Malaysia to include this warning into the local prescribing information and to inform all healthcare professionals of this labeling update through a Dear Healthcare Professional Letter.

Reference:

1. Medwatch, U.S.F.D.A., http://www.fda.gov/medwatch/safety/2008/safety08.htm#exubera

REGULATORY MATTERS

INCIDENCE OF MYOCARDIAL INFARCTION IN PREGNANT WOMEN RECEIVING BETA AGONIST TO DELAY PRE – MATURE LABOUR – ADDITIONAL WARNING AND PRECAUTION

GlaxoSmithKline in Canada has recently informed all healthcare professionals of the result of its recently conducted review on safety data concerning Ventolin® I.M. Injection and Ventolin® I.V. infusion solution (salbutamol sulphate for injection) when used in pregnant women to delay pre – mature labour. The review was done on published literature, spontaneous reports and clinical trials. It was found that up to the end of April 2007, there have been 17 worldwide cases related to salbutamol causing myocardial ischaemia when used to delay premature labour. Eleven of the reports were serious (included 1 fatality). Twelve patients recovered without sequelae.

Most of the reports involved patients using parenteral formulations and none using inhaled salbutamol formulation for the treatment of bronchospasm. From the review, if the benefit of using salbutamol in women in premature labour outweighs the risk, healthcare professionals were advised to monitor the patient's fluid balance and cardio – respiratory function, including ECG monitoring. If signs of pulmonary oedema or myocardial ischaemia develop, treatment should be discontinued.

Salbutamol is not indicated to stop or prevent premature labour in Canada. However, Health Canada instructed that all salbutamol injectables are required to include:-

Warnings and Precautions:

Pregnant Women

- *Salbutamol, in common with other betamimetics, is not approved to stop or prevent premature labour.*
- *Due to the risk of pulmonary edema and myocardial ischemia that has been observed during the use of betamimetics in the treatment of premature labour, before PrVENTOLIN ® injections are given to any patient with known heart disease, an adequate assessment of the patient's cardiovascular status should be made by a physician experienced in cardiology.*

Labour and Delivery

- *Cautious use of PrVENTOLIN® injections is required in pregnant patients when it is given for relief of bronchospasm so as to avoid interference with uterine contractibility. During I.V. infusion of salbutamol, the maternal pulse rate should be monitored and not normally allowed to exceed a steady rate of 140 beats per minute.*

- *As maternal pulmonary edema and myocardial ischemia have been reported during or following premature labour in patients receiving beta$_2$-agonists, careful attention should be given to fluid balance and cardio-respiratory function, including ECG monitoring. If signs of pulmonary edema or myocardial ischemia develop, discontinuation of treatment should be considered.*

In reviewing these safety concerns, the DCA also sought feedback from local practitioners and received comments from two Obstetrics and Gynaecology Specialists that a number of products, including salbutamol and terbutaline products were used to delay pre – mature labour in women. These specialists were of the opinion that besides salbutamol, terbutaline can also cause similar complications.

In Malaysia, the DCA has registered beta – agonists (salbutamol and terbutaline) for such indication. There are 82 registered products that contain salbutamol (26 products of oral tablets/capsules, 28 products of syrups/ suspensions, 23 products for inhalation, 4 products of injectables and 1 product for nebulization) and 30 registered products containing terbutaline (8 products of oral tablets/capsules, 16 products of syrups/suspensions, 5 products for inhalation and 1 injectable).

Hence, the DCA has instructed the registration holders of all oral tablets/capsules and injectables salbutamol and terbutaline (syrups, suspensions and inhalation products are exempted) to include the following into the "Warnings and Precautions" section of the product's information leaflet:-

For injectables:

- As maternal pulmonary oedema and myocardial ischaemia have been reported during or following premature labour in patients receiving beta$_2$ – agonists, careful attention should be given to fluid balance and cardio-respiratory function, including ECG monitoring. If signs of pulmonary oedema and myocardial ischaemia develop, discontinuation of treatment should be considered.
- Due to the risk of pulmonary oedema and myocardial ischaemia that has been observed during the use of beta$_2$-agonists in the treatment of premature labour, before these products are given to any patient with known heart disease, an adequate assessment of the patient's cardiovascular status should be made by a physician experienced in cardiology.
- Cautious use of salbutamol/terbutaline injections is required in pregnant patients when it is given for relief of bronchospasm so as to avoid interference with uterine contractibility. During IV infusion of salbutamol/ terbutaline, the maternal pulse should be monitored and not normally allowed to exceed a steady rate of 140 beats per minute.

For tablets and capsules:

- As maternal pulmonary oedema and myocardial ischaemia have been reported during or following premature labour in patients receiving beta$_2$ – agonists, careful attention should be given to fluid balance and cardio-respiratory function, including ECG monitoring. If signs of pulmonary oedema and myocardial ischaemia develop, discontinuation of treatment should be considered.
- Due to the risk of pulmonary oedema and myocardial ischaemia that has been observed during the use of beta$_2$-agonists in the treatment of premature labour, before these products are given to any patient with known heart disease, an adequate assessment of the patient's cardiovascular status should be made by a physician experienced in cardiology.

Healthcare professionals are advised to take precaution when using beta – agonists to delay pre – mature labour in women and to report any adverse drug reactions to the DCA, if encountered.

References:

1. Health Canada, Advisories, Warnings and Recalls for Health Professionals, http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2007/ventolin_nth-aah-eng.php
2. MADRAC's Database

3. Opinion of Obstetric and Gynaecology Specialists, Dato' Dr. Ravidran Jegasothy, Head of Obstetric and Gynaecology Department, Hospital Kuala Lumpur
4. Opinion of Obstetric and Gynaecology Specialists, Dr. S. Sevellaraja, President, Obstetrical and Gynaecological Society of Malaysi

LOW MOLECULAR WEIGHT HEPARIN (LMWH) – CLEXANE® PREFILLED SYRINGES (ENOXAPARIN)

Background

The USFDA reported that there was an increase in the number of ADRs associated with the use of some multidose heparin sodium products this recent February 2008. The ADRs reported were "allergic/anaphylactoid type symptoms (including profound hypotension, bronchospasm and gastrointestinal symptoms)". Some of the reports were serious while a few of them resulted in fatalities. Similar ADRs were also reported in Germany. The batches of products that were suspected to cause these ADRs were recalled from the market.

Initial investigations revealed that the involved batches were contaminated with "over – sulphated chondroitin sulphate" (OSCS) where the crude heparin and active ingredient was porcine – based and sourced from China and the United States of America. This contaminant has the same structure as heparin but it is not naturally occurring nor a by – product from manufacturing processes.

On the 18 April 2008, the Spanish Agency for Medicine and Healthcare Products issued a "Rapid Alert Notification of a Quality Defect/Quarantine" on contamination which involved Clexane®, a Low Molecular Weight Heparin (LMWH). The market authorization (registration) holder for Clexane® in Malaysia was instructed to give feedback on the status of contamination of all batches available in Malaysia. The feedback stated that globally, there were a few batches of Clexane® that were contaminated with OSCS. The contamination is classified into four categories:

- Category A – not detected: <1%
- Category B – detected and not quantified: 1 – 2%
- Category C – quantitatively determined: 2 – 5%
- Category D – quantitatively determined: > 5 – 7%

In some countries such as United Kingdom, France, Ireland, Hungary, Slovakia, India, Germany, Italy and Indonesia, marketing and use of category B products have been allowed. However, in Australia, Spain, Denmark and Austria, products identified with category B and C levels of contamination are not allowed to be used. Products with category B, C and D contaminations were recalled and quarantined.

There have been no reports of an increase in trend for adverse reaction reporting globally even after Category B products were used in some countries.

The Situation in Malaysia

Feedback from the manufacturer on the status of Clexane® in Malaysia indicated that one batch each of Clexane® 4000 IU and 6000 IU prefilled syringe had been identified to be contaminated with OSCS at Category B level. The stocks had not been released and would continue to be quarantined at the warehouse.
In Malaysia, up till June 2008, MADRAC received 39 suspected ADR reports associated with the use of Clexane®. Three of these reports were received in 2008 and none of the reported reactions were indicative of "anaphylaxis".

A meeting was held between the chairman of MADRAC and medical specialists recommended by the Ministry of Health to discuss this issue of OSCS contamination of Clexane® and the available options to manage the possible shortage of LMWH that could arise due to the global situation. The meeting was of the consensus that Malaysia should avoid using Clexane® products of category B, C and D contamination.

The DCA was duly informed of this recommendation and deliberated on this matter at its 205th Meeting. It was agreed that the market authorization holder of Clexane® was to be informed that only category A products can be supplied by the company and instructed that any category B stocks (4000IU and 6000IU) that are still in the warehouse should be quarantined and not allowed to be distributed to any hospital. Healthcare professionals in both the private and public sectors have been informed of this decision.

References:

1. Spanish Agency for Medicine and Healthcare Products, “Rapid Alert Notification of a Quality Defect/ Quarantine”, 18 April 2008.
2. http://www.mhra.gov.uk/PrintPreview/DrugALertSP/CON014890
3. http://www.tga.gov.au/alerts/medicines/clexane.htm

CARDIAMED® (NORADRENALINE) - AN UPDATE

The MADRAC had received 7 ADRs reports which involved the use of noradrenaline (Cardiamed®) from two different hospitals. The patients developed gangrene on the toe(s)/finger(s)/leg and/or peripheral cyanosis 2 to 5 days post injection. It was initially suspected that the dosing and/or method of administration could be possible contributory factors towards the adverse events reported. However, after gathering more information from the reporters, it was found that the dosing and method of administration was as per recommendation.

Discussions were conducted with the manufacturer of Cardiamed® who agreed to do a voluntary recall of Cardiamed® with the batches KKM 27177, KKM 27162 and KKM 27165 in view of potential patient safety concerns due to the reported adverse events. This was duly done on the 10 April 2008.

During the 205th DCA meeting, members of the DCA agreed to suspend the registration of Cardiamed®.

The MADRAC will continue to monitor if such ADRs occur with other noradrenaline products that are registered with the DCA.

LOCAL CASE REPORTS

DRUG EXPOSURE DURING PREGNANCY – OLANZAPINE

A 32-year-old Asian female patient with a medical history of schizophrenia was reported to be taking olanzapine 5mg daily beginning on an unspecified date in 2001 for her condition. Her past medical history included the use of haloperidol for schizophrenia.

It was unknown if the patient was taking olanzapine at the time of conception. However, the patient received olanzapine during all three trimesters of her pregnancy. The estimated due date was 26 November 2007. Her psychiatrist stopped her treatment for two weeks at an unspecified date. However, the patient experienced a relapse of her condition after olanzapine was stopped and requested for the olanzapine treatment to be restarted. The psychiatrist, considering the risk-benefit profile, restarted the patient on olanzapine 2.5mg daily.

On 20 November 2007, the patient delivered a male infant at 40 weeks gestation. The infant weighed 3kg. The infant was born with no ear lobe on the right side and hypospadias.

KISAN® INJECTION 10MG/ML

Kisan® Injection 10mg/mL contains phytomenadione, commonly known as Vitamin K.

In October 2007, the DCA received two ADRs reports from a government hospital which involved Kisan®. The patients experienced “shortness of breath”, “faint”, “erythema”, “itchiness”, “anaphylactic shock” and “angioedema” with a very rapid onset. The MADRAC has given a “C2” causality grading for these two reports.

In February 2008, another ADR report was received from the same hospital on this product. The patient experienced “shortness of breath”, “giddiness”, “hypotension” and “vomiting” after this injection was given. The MADRAC has given this report a “C2” causality grading.

Investigations were carried out to determine the possible causes of these reported ADRs, including looking at product formulation, methods of administration and so on.

The formulation of Kisan® includes cremophor EL. Cremophor EL or its common name Polyoxyethylated castor oil (a non – ionic emulsifying agent used to prepare stable injectable liquid preparations of drugs with low aqueous solubility) is used as a stabilizer for this formulation. This ingredient was found to be able to cause "severe anaphylactoid reactions" and is listed as one of the ingredients in the *WHO Consolidated List of Products, Eight Issue Pharmaceuticals*. However, this ingredient is still being used in some countries while others have banned its use following cases of "severe anaphylactoid reactions" associated with it. In Malaysia, Cremophor EL is allowed to be used.

In the product information leaflet, "anaphylaxis" is stated as one of the side effects of using Kisan®. However, it did not state that Cremophor EL can cause so. It was also stated in the product information leaflet that Kisan® has to be given "*by very slow intravenous injection, at a rate not exceeding 1mL/minute*"

Through the investigations, it was found that the patients were given bolus injections. The hospital has been advised not to do so and to disseminate this information to all the healthcare professionals. Other hospitals were also contacted to check if such ADRs had occurred in their hospitals.

A reminder on the proper recommended method of administration for Phytomenadione/Vitamin K injections; must be infused by **VERY SLOW INTRAVENOUS INJECTION** and **NOT BY BOLUS** has been circulated to all hospitals. Besides that, the manufacturer has agreed to labeling changes to emphasize and clearly state that Kisan® cannot be infused via bolus injections in the package insert, ampoule label as well as the outer label of the product.

References:

1. Kisan® Injection 10mg/mL Injection Product Information Leaflet.
2. WHO Consolidated List of Products, Eight Issue Pharmaceuticals

A REMINDER: METOCLOPRAMIDE – USAGE IN CHILDREN

The World Health Organization (WHO) Pharmaceutical Newsletter, No. 2, 2007 reported that the Netherlands Medicines Evaluation Board (MEB) has decided to restrict the use of metoclopramide in children. This is following to the increased risk of extrapyramidal symptoms in children receiving metoclopramide. MEB suggested that metoclopramide should be used only in treatment of severe nausea and vomiting of known origin, and only if the treatment with other products is ineffective or it is not possible. The MEB suggested that there are better alternatives to metoclopramide such as domperidone and 5-HT3 receptor antagonists to treat post – operative nausea in children because the risk of extrapyramidal effects is lower.

In August 2007, the MADRAC has requested the Pharmaceutical Services Division, Ministry of Health to disseminate this information to healthcare professionals. The MADRAC newsletter also had coverage on this matter in the September 2007 issue.

However, reports of such ADRs happening in children are still received by MADRAC due to the continued usage of metoclopramide in children. From January 2007 to June 2008, the MADRAC received 13 adverse drug reactions reports involving children using metoclopramide. Among the adverse drug reactions reported were oculogyric crisis (5), neck stiffness (2), torticollis (1), muscle stiffness (1), eyes gaze upward/eyes rolling (5) and back stiffness (1).

Hence, a reminder of this safety concern was issued in April 2008 to all healthcare professionals via the Pharmaceutical Services Division, Academy of Medicine, Malaysian Medical Association, Association of Private Hospital Malaysia and Malaysian Pharmaceutical Society. The MADRAC will continue to monitor the situation and further regulatory action will be taken, if deemed necessary.

References:

1. WHO Pharmaceutical Newsletter, No.2, 2007
2. MADRAC's Database.