EDITORIAL

In this edition several topical issues are brought to the attention of our readers. Long-term use of hormone replacement therapy is discouraged on the basis of a large observational study of nearly a million postmenopausal women, which showed an increased incidence of fatal breast cancer. Whereas nimesulide, which has been a subject of concern due to its association with hepatic reactions, has received a favourable benefit/risk assessment by the European Committee for Proprietary Medicinal Products. A new antimalarial drug combination (chlorproguanil-dapsone) was approved by the UK Medicines and Healthcare Products Regulatory Agency (MHRA) for treating uncomplicated *Plasmodium falciparum* malaria. It is intended to be used in sub-Saharan Africa.

A European-Pacific kava strategy meeting was held in Brussels, Belgium on 25-26 August. This meeting sought to address issues on the implications of the ban on "synthetic" kava preparations on the use of natural kava products. A full report on this issue will be forthcoming later.

The first meeting of the WHO Advisory Committee for the Safety of Medicinal Products (ACSoMP) will take place in Geneva in the month of October. This is an important development since the remit of the Committee is to set a policy for WHO in the area of medicine safety and to review controversial safety issues. In December, the National Centres for Pharmacovigilance will get together in New Delhi, India for their annual meeting. Further information on this will shortly be available on the website: http://www.who-umc.org.
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ABACAVIR, LAMIVUDINE, TENOFOVIR

Virologic non-response in HIV with combination therapy

Europe, USA. The EMEA, US FDA and Swissmedic are informing physicians of reports of a high rate of early virologic non-response observed in a GlaxoSmithKline (GSK)-sponsored clinical study of therapy naïve adults receiving once daily three drug combination therapy with tenofovir (Viread), lamivudine (Epivir) and abacavir (Ziagen). The precise nature of any interaction leading to non-response is currently unknown. The Marketing Authorization Holders have been requested to further explore the nature of these interactions through in vivo/in vitro studies. In the meanwhile physicians are advised that,

- abacavir and lamivudine, in combination with tenofovir should not be used as a triple antiretroviral therapy when considering a new treatment regimen for naïve or pre-treated patients, particularly as a once-daily regimen
- patients currently controlled with this combination should be frequently monitored with a sensitive viral load test and considered for modification of therapy at the first sign of viral load increase.

GlaxoSmithKline has issued a ‘Dear Healthcare Provider’ letter for the above information. Patients about to receive or, currently on this combination therapy are advised to inform their physician immediately.

Reference:

ACETYLSALICYLIC ACID (PAEDIATRIC) OTC withdrawal

Spain. The Spanish Medicines Agency has announced that, starting 20th June 2003, all paediatric OTC medicinal preparations containing salicylates/acyetlsalicylic acid (Aspirin) are being withdrawn from the market. This measure has been undertaken to prevent the use of these products in children with viral fever and thereby reduce the risk of Reye’s syndrome in these children. For non paediatric OTC products containing salicylates/acyetlsalicylic acid the Summary of Product Characteristics (SPC) will have to be modified to include the following:

- salicylates/acyetlsalicylic acid – containing OTC products for adult use are contraindicated in children below the age of 16 years
- salicylates/acyetlsalicylic acid – containing prescription products are contraindicated for the treatment of fever, chickenpox and viral fevers in patients below 16 years of age.

Reference:

ACETYLSALICYLIC ACID, PARACETAMOL, IRON

New packaging standards for improving child resistance

UK. The Medicines and Healthcare products Regulatory Agency (MHRA) in the UK has announced that all products containing acetylsalicylic acid, paracetamol and iron will now be required to be in packaging that meets the new British Standard on child resistance for medicines. The new regulations will come into force on 1 October 2003 with a 2-year transitional period for products already on the market to comply. The proposal endorses an additional safeguard in keeping medicines out of children’s reach and is based on a 12-week public consultation exercise involving Pharmacy Colleges, the National Health Service, Industry, Medical Colleges and other professional bodies.

Reference:

BENZBROMARONE

Withdrawn due to reports of liver damage

France. Sanofi-Synthélabo has withdrawn its hypouricaemic product benz bromarone (Desuric) in France following reports of serious liver damage associated with the product’s use. Benz bromarone (Desuric) has been marketed in France since 1976, but rare reports of serious cytolytic liver damage, including fatal cases and others requiring liver transplants, have led to an unfavourable benefit/risk ratio. The company has therefore decided to stop the marketing of this product in France and to recall all stocks.

Reference:
**REGULATORY MATTERS**

**EZETIMIBE**

Labelling update regarding hypersensitivity reactions

**USA.** Merck/Schering-Plough Pharmaceuticals have issued a press release in which they note the addition of information regarding reports of hypersensitivity reactions to the labelling of their lipid-lowering agent ezetimibe (Zetia). The Adverse Reactions section of the product labelling has been updated following reports of hypersensitivity reactions, including rash and angioedema, all of which either resolved spontaneously or were successfully treated with standard therapies. In the release, Merck/Schering-Plough note that many commonly used drugs list hypersensitivity reactions, including angioedema, in the Adverse Reactions sections of their product labels, including the most widely prescribed lipid-lowering agents. They point out that, unlike other lipid-lowering drugs, clinical trials of ezetimibe (Zetia) showed no increased risk of myopathy or rhabdomyolysis.

Reference:

**LEFLUNOMIDE**

Explicit liver function monitoring directions added to label

**USA.** Leflunomide (Arava) labelling in the US now includes more explicit liver function monitoring directions. The label now states that at the minimum, ALT must be performed at baseline and monitored initially at monthly intervals during the first six months and then, if stable, every six to eight weeks thereafter. The label previously recommended monthly monitoring until stable without mention of the 6-month timeframe or frequency of monitoring once stable. In addition, a bolded statement on severe liver injury has been added to the Warnings section and the manufacturer (Aventis) is to issue a ‘Dear Healthcare Professional’ letter regarding the labelling changes.

Reference:

**PAROXETINE**

Unfavourable risk benefit ratio in children and adolescents

**UK, Canada.** New data from clinical trials of paroxetine (Seroxat) in children and adolescents received by the UK Medicines and Healthcare products Regulatory Agency (MHRA) do not show a favourable risk/benefit profile of paroxetine in this age group. According to the Committee on Safety of Medicines these data do not demonstrate efficacy in the treatment of depressive illness and show an increase in the risk of harmful outcomes, including episodes of self-harm and potentially suicidal behaviour; the risk of these outcomes appears to be 1.5−3.2 times greater in those receiving paroxetine than in those receiving placebo. The CSM has therefore advised that paroxetine should not be used in children and adolescents under the age of 18 years to treat depressive illness. The product information for paroxetine (Seroxat) is to be updated accordingly1. Health Canada has also advised that the product monograph for paroxetine (Paxil) be updated with similar information in Canada. Although paroxetine (Paxil) is not indicated for use in patients under 18 years of age in Canada, the off-label use of the product exists in the paediatric population. Health Canada also warns that paroxetine should not be abruptly discontinued but should be gradually tapered off to avoid discontinuation symptoms.

Reference:

**SALMETEROL**

Risk of life-threatening asthma episodes

**USA.** The US FDA is advising that all drug products containing salmeterol will now include new safety information and warnings about a small but significant number of reports of life-threatening asthma episodes or asthma related deaths in patients taking these products. Salmeterol is a long-acting bronchodilator used to treat asthma and chronic obstructive pulmonary disease (COPD). The FDA announcement follows the findings of a large safety study in the US showing a significant increase in respiratory-related death or life-threatening experience in African-American patients treated with the drug (Serevent). However, the FDA emphasizes that based on available data, the benefits of treatment with salmeterol in patients with asthma and COPD continue to outweigh the potential risks when used according to the instructions contained in the product labelling. Patients should not stop taking products that contain salmeterol, or any other medication for asthma or COPD without consulting their physicians since abrupt discontinuation of therapy can result in worsening of the disease with serious and fatal consequences.

Reference:
SOMATROPIN (rDNA ORIGIN)

Reports of fatalities in paediatric patients with Prader-Willi syndrome

USA. Pharmacia & Upjohn Company, in association with the US FDA is informing healthcare professionals about seven post marketing reports of fatalities associated with the use of growth hormone in paediatric patients with Prader-Willi syndrome. These patients had one or more of the following risk factors including severe obesity, history of respiratory impairment or sleep apnoea, or unidentified respiratory infection. In view of these observations the Contraindications section now warns that growth hormone is contraindicated in patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment. The package insert also warns about the reports of fatalities in paediatric patients with one or more of the above mentioned risk factors. The warnings section also informs that male patients (with one or more risk factors) may be at greater risk. Patients with Prader-Willi syndrome should be evaluated for upper airway obstruction before initiation of treatment and treatment with growth hormone should be discontinued if airway obstruction develops during treatment. All patients with Prader-Willi syndrome should have effective weight control, evaluated for sleep apnoea and monitored for signs of respiratory infections.

Reference:

TOPIRAMATE

Risk of oligohidrosis and hyperthermia

USA, Canada. Ortho-McNeil Pharmaceutical Inc in the USA and Janssen-Ortho Inc in Canada are warning healthcare professionals about rare reports, primarily in children, of oligohidrosis (decreased sweating) and hyperthermia in patients treated with topiramate (Topamax). Most cases occurred in association with exposure to elevated temperatures and/or energetic activity. The prescribing information for topiramate (Topamax) has been updated to reflect these reports. Oligohidrosis and hyperthermia may have potentially serious sequelae and may be preventable by prompt recognition of symptoms and appropriate treatment. Patients on topiramate therapy should be closely monitored for signs of decreased sweating and increased body temperature, and when topiramate is prescribed with other drugs such as carbonic anhydrase inhibitors and anticholinergics that can predispose patients to heat-related disorders.

Reference:
1. ‘Dear Healthcare Professional’ letter from Ortho-McNeil, 09 Jul

TIROFIBAN

Advice against off-label use

Malaysia. The Drug Control Authority (DCA) in Malaysia has directed the manufacturer of tirofiban (Aggrastat) to issue a ‘Dear Doctor’ letter advising health professionals against the off-label usage of tirofiban (Aggrastat) injection. This advice follows reports of fatal outcomes occurring with the use of tirofiban with heparin during cardiopulmonary bypass in patients who previously experienced heparin-induced thrombocytopenia type II reactions.

Reference:

Reports in WHO-file:
Sweating decreased 9, hyperpyrexia 3, hyperpyrexia malignant 1

Reference:
ATYPICAL ANTI-PSYCHOTICS

Reports of hypertension

New Zealand. The Intensive Medicines Monitoring Programme (IMMP) in New Zealand has led to the identification of associations between atypical antipsychotics and hypertension. A total of 572 case reports involving atypical antipsychotics were analysed and hypertension was identified as a possible adverse drug reaction (ADR). Hypotension, a known side effect, was reported in 19 cases, compared with 13 cases of hypertension, involving clozapine (n = 10), risperidone (2) and quetiapine (1). The two most severe cases occurred with risperidone: two women, aged 53 and 54 years, received risperidone 1 and 0.5 mg/day, respectively, for 3 days before experiencing increases in blood pressure (BP) to 190/110 and 210/110mm Hg, respectively; both patients recovered shortly after risperidone discontinuation. In the 11 other cases, patients aged 15−66 years developed marked increases in BP with systolic pressures of 140−170mm Hg and diastolic pressures of 95−120mm Hg. In all but one case, BP elevation occurred within 1 month of starting treatment. 4 of the 13 patients were receiving concomitant SSRIs. According to the Director of the programme, Dr David Coulter “the evidence from these case reports is sufficient to establish a signal of a reaction that seems little known”. He says that it would be prudent to monitor BP during the start of atypical antipsychotic treatment, especially in patients receiving concomitant SSRIs.

Report in WHO-file: Clozapine 648, risperidone 185, quetiapine 25

Reference:

BOTULINUM A

Patients misled over safety

USA. The US FDA has raised objections that the web advertising or the product information in print for botulinum A toxin preparation (Botox) as posted by the company (Allergan) has insufficient information on the unwanted side effects that could result in patients treated with the product for cosmetic purposes. FDA is of the opinion that the advertisements pertaining to the product are false and misleading because they falsely identify the product as a cosmetic treatment, fail to reveal material facts about the product use and minimise the risk information presented. The advertising does not make it clear that more than four in ten people treated with the product suffer some form of side effect. The most common side effects of the treatment are headache and nausea; the product has also been linked with respiratory infection and ‘flu syndrome’, as well as temporary drooping of the eyelids.

Reference:

CHELIDONIUM MAJUS

Statement to advise use under supervision

Australia. The Complementary Medicines Evaluation Committee (CMEC) has advised that all oral C.majus (Greater celandine/Chelidonium) products should contain a label with the warning that the products should be used under the supervision of healthcare professionals. Consumers with a history of liver disease should seek advice from a healthcare professional before commencing use and to discontinue use if particular symptoms occur. This recommendation follows the CMEC’s careful examination of all available evidence linking ingestion of C.majus with moderate to severe, reversible acute hepatitis in a relatively small number of individuals worldwide. The mechanism underlying the hepatotoxic effect needs to be elucidated. Pending further information, the Therapeutic Goods Administration (TGA) has advised healthcare professionals to be vigilant to signs of liver toxicity associated with the use of Chelidonium-containing medicines. C.majus (Greater celandine) has been traditionally used to treat a range of conditions including liver disorders and is available internationally.

Reference:

CYCLO-OXYGENASE (COX)-2 INHIBITORS

Reports of hepatotoxicity

New Zealand. Seventeen reports of hepatotoxicity have been received as part of the IMMP (Intensive Medicines Monitoring Programme) monitoring of selective COX-2 inhibitors, including three reports of significant liver injury in patients aged 85, 81 and 61 years, who received rofecoxib for 7 days to 3 months before developing liver injury, ranging from markedly elevated liver transaminase levels to biopsy-confirmed severe cholestatic hepatitis. There were also three similar reports of liver injury in patients receiving celecoxib, although the association was less clear due to concomitant medications. The remaining reports involved mild liver function abnormalities with celecoxib (n = 8) and rofecoxib (3). The IMMP reports of hepatotoxicity with COX-2 inhibitors suggest that ‘this type of reaction is an uncommon class
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effect of all NSAIs (nonsteroidal anti-inflammatory agents), both COX-2 specific and non-specific.’

Reports in WHO-file:
Coxibs; Liver and biliary system disorders 891

Reference:
Prescriber Update 24(1): Jun 2003. Available from URL:
http://www.medsafe.govt.nz

ETONOGESTREL
Vaginal bleeding with sub-dermal implant

Australia. Since August 2001, the Adverse Drug Reactions Advisory Committee (ADRAC) has received 130 reports of adverse reactions associated with the sub-dermal etonogestrel contraceptive implant (Implanon). Thirty-seven of the reports described prolonged vaginal bleeding of 2–26 weeks duration (median 8 weeks) which generally started soon after insertion, but in some cases after up to 16 weeks. Thirty-three of the 37 cases required removal of the implant; one patient was hospitalised and required 4 units of packed RBCs. The Committee notes that, in a published 3-year study of sub-dermal etonogestrel implant (Implanon), heavy or prolonged bleeding was experienced by 2.8% of patients.

Reports in WHO-file:
Vaginal haemorrhage 65

Reference:

FLUTICASONE
ADR update

New Zealand. The Medicines Adverse Reactions Committee (MARC) in New Zealand has added adrenal insufficiency, hypoglycaemia or seizure associated with inhaled fluticasone propionate (Flixotide) to the list of adverse reactions of current concern. This follows concerns arising from international reports of these adverse events in association with inhaled fluticasone propionate (see WHO Pharmaceuticals Newsletter No.3, 2003). MARC notes that, although adrenal insufficiency may occur with any inhaled corticosteroid, it may be more common with fluticasone propionate because of its greater potency.

Reference:

GATIFLOXACIN
Reports of abnormal glucose metabolism

Canada. Health Canada received 28 reports (44% of all gatifloxacin reports) of abnormal glucose metabolism associated with gatifloxacin (Tequin) between February 2001 and February 2003, of which 19 were of hypoglycaemia, seven were of hyperglycaemia and two were of both hypo- and hyperglycaemia. Twenty-five of the cases involved patients with type 2 diabetes mellitus, and 18 of the 19 cases of hypoglycaemia involved the concomitant use of a hypoglycaemic agent. All 28 cases were serious; 19 patients required new or prolonged hospitalisation and two patients (aged 86 and 102 years) died.

Reports in WHO-file:
Hypoglycaemia 164, hyperglycaemia 79, diabetes mellitus 7, diabetes mellitus aggravated 17

Reference:

HORMONE REPLACEMENT THERAPY (HRT)
‘Million Women Study’ confirms breast cancer association

UK. The Million Women Study sought to examine the effect of different types of HRT and tibolone (a synthetic HRT: Livial), on the risks of breast cancer in nearly a million postmenopausal women in the UK over a period of five years. According to the Committee on Safety of Medicines (CSM), an analysis of the study results shows that
• the previously described small increase in risk of breast cancer in association with oestrogen-only products stands confirmed
• the increased risk of breast cancer in association with the use of combined (oestrogen plus progestogen) HRT is substantially higher than with oestrogen-only therapy
• tibolone (Livial) also significantly increases the risk of breast cancer, but to a lesser extent than combined HRT
• an increase in the risk of breast cancer becomes apparent within 1-2 years of starting treatment and that
• the risk of breast cancer begins to decline when HRT is stopped and by 5 years reaches the same level as in women who have never taken HRT.

The CSM advises that the benefits of short-term HRT for menopausal symptoms outweigh the risks for many women. For longer term use of HRT, women should be made aware of the increased incidence of breast cancer and other adverse effects. Each decision to start HRT should be made on an individual basis and the treatment should be reappraised regularly, at least once a year.

Reference:

WHO Pharmaceuticals Newsletter No. 4, 2003 • 5
MEDROXY-PROGESTERONE

Reports of contraception failure with depot preparations

Australia. The Adverse Drug Reactions Advisory Committee (ADRAC) has received 27 reports of women becoming pregnant despite using depot medroxyprogesterone (Depo-Provera, Depo-Ralovera) for contraception. In 10 cases, the women became pregnant 2 – 10 weeks after administration of the drug. An interaction between medroxyprogesterone and carbamazepine was suspected in two cases, while in another nine cases the injections were given late or at borderline times. The committee says that prescribers and healthcare professionals should avoid the following situations which may contribute to the risk of contraceptive failure: incorrect timing of the injection, failure to properly suspend the microcrystals before injection, failure to dispense the full dose, incorrect injection technique or injection of the incorrect drug.

Reports in WHO-file:
Pregnancy unintended 349
Reference:

MEFLOQUINE

Patient guide warns of psychiatric adverse events

USA. The US FDA, in collaboration with Roche Pharmaceuticals, has developed a Medication Guide (US FDA-approved patient labelling) for the antimalarial agent mefloquine (Lariam); it includes the addition of a warning that, in rare cases, the drug has been associated with severe psychiatric events such as suicidal thoughts. The guide will provide improved information on the risks and benefits associated with the use of mefloquine (Lariam) and educate patients about how to optimise the drug’s effectiveness. It will help ensure patients understand the risk of rare but potentially serious psychiatric adverse events associated with the use of mefloquine (Lariam) and will contain information on how patients can recognise the psychiatric risks and take early action to avoid serious harm. Specifically, the guide instructs patients who experience a sudden onset of anxiety, depression, confusion or restlessness to see a physician or other healthcare provider, as it may be necessary to discontinue mefloquine (Lariam). It also notes that there have been rare reports of suicidal thoughts and more rarely, of suicide in mefloquine (Lariam) users, although a relationship with the drug has not been established.

Reference:

METHOTREXATE

New solutions to prevent fatalities/ adverse events

UK. The National Patient Safety Agency (NPSA) has announced a package of practical solutions to reduce errors associated with the use of oral methotrexate. Oral methotrexate tablet is taken as a weekly dose by thousands of people in the UK for the treatment of moderate to severe rheumatoid arthritis and severe psoriasis. The weekly dosing regimen raises opportunities for dosing errors, with errors occurring during the transfer of information from hospitals to GPs and due to problems with information technology support systems that fail to give clear information on the frequency of dosing. The NPSA has identified 25 deaths and 26 cases of serious harm linked to improper use of oral methotrexate in a community setting over a 10-year period in England. The National Patient Safety Agency (NPSA), in collaboration with health professionals, patient groups and pharmaceutical suppliers, has proposed 3 national solutions:

1. A new patient treatment diary with complete information to empower patients with appropriate knowledge and help keep their own track record (for frequency of dosing, monitoring etc).

2. New packaging designs with a view to help improve safety when methotrexate is prescribed by healthcare staff and administered by patients and their carers.

3. A project to adapt IT systems in GP surgeries and community pharmacies to incorporate flagging mechanisms and default settings to support staff by designing out opportunities for human errors in prescribing the drug.

These solutions will be developed in collaboration with the major stakeholders and subject to further testing and risk assessment by the NPSA.

Reference:

MINOCYCLINE

Hepatic reactions

Australia. The Adverse Drug Reactions Advisory Committee (ADRAC) in Australia has received 42 reports of hepatic reactions, including 21 of hepatitis, associated with minocycline; in most cases minocycline was the sole suspected drug. In 28 cases
minocycline was being used to treat acne and 15 of the 42 patients were less than 21 years old. Of the 42 cases, 25 had recovered by the time of reporting, most within 12 weeks of stopping minocycline; none of the patients died or required liver transplantation. The Committee notes that five cases were suggestive of an autoimmune reaction, with antinuclear antibodies and, in one case, features of lupus erythematosus. Prescribers are advised that hepatitis in a patient receiving long-term minocycline may be indistinguishable from autoimmune hepatitis; however, discontinuation of minocycline usually results in complete recovery.

Reports in WHO-file: Liver and biliary system disorders 600

Reference:

RIFAMPICIN & PYRAZINAMIDE

Warning against use in latent tuberculosis

USA. The US Federal health officials are warning physicians against prescribing rifampicin-pyrazinamide combination for the treatment of tuberculosis (TB) due to reports of severe liver toxicity and death in some patients. 11 patients with latent TB died between October 2000 and June 2003 and another 37 patients were hospitalised with liver injuries after being treated with the combination. The Centers for Disease Control and Prevention (CDC) advise that a nine-month course of isoniazid is the preferred treatment option for latent TB, especially in patients with alcoholism or liver problems. However the combination could be considered in patients with active TB or in patients unlikely to complete a nine-month course of isoniazid.

Reference:

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs):

Reports of hyponatraemia

Australia. The Adverse Drug Reactions Advisory Committee (ADRAC) has now received a total of 311 reports of hyponatraemia associated with the use of SSRIs and venlafaxine; in 67 of these reports the patient also had the syndrome of inappropriate antidiuretic hormone secretion. An SSRI was the only suspected drug in more than two-thirds of the 311 reports, although a small proportion (14%) of cases involved the concurrent use of a diuretic. The majority (75%) of patients were women and most (85%) were older than 60 years (mean age 77 years). Hyponatraemia usually occurred within the first 30 days of use and in many cases was the only abnormality reported, with a median serum sodium nadir of 120 mmol/L (range 113–133). Approximately two-thirds of cases recovered fully after withdrawal of the SSRI and fluid restriction, but three cases had a fatal outcome.

Reports in WHO-file: SSRIs: Hyponatraemia 2381

Reference:

SIBUTRAMINE

Serotonin syndrome

Canada. Between February 2001 and December 2002, Health Canada received 87 reports of adverse reactions associated with the use of sibutramine (Meridia), three of which described serotonin syndrome. Sibutramine was taken concomitantly with fluoxetine in one case and with sertraline in another; none of the cases were fatal. Health Canada points out that the concomitant use of sibutramine and other agents with serotonergic activity is contraindicated in the Canadian product monograph for sibutramine (Meridia), but notes that eight of the 87 cases involving sibutramine reported the concomitant use of SSRIs or other serotonergic drugs.

Reference:

TICLOPIDINE

No decrease in ADR reports

Japan. The number of reports of adverse drug reactions (ADRs),
including death due to the antiplatelet agent ticlopidine has not decreased despite the second ‘Dear Doctor’ letter distributed last July in Japan. The number of reports of serious ADRs also remains unchanged. The first letter was issued in 1999 following a series of reports of deaths due to thrombotic thrombocytopenic purpura, agranulocytosis, and serious hepatic dysfunction. Medical institutions were strongly requested to conduct haematological and hepatic function tests after starting administration because severe adverse reactions were found to occur especially in this period. Despite these measures 145 episodes of serious ADRs, including 17 deaths were reported between July 2001 and June 2002. This led to the second ‘Dear Doctor’ letter being issued at the end of July 2002. However, the situation has not improved even with the second letter.


**VIGA/VIGA FOR WOMEN**

**Presence of sildenafil**

USA. Health Nutrition (RMA Laboratories), under advice from the US FDA is warning consumers not to purchase or consume the product known as VIGA or VIGA FOR WOMEN. These products are sold as dietary supplements, without a medical prescription and have been found to contain sildenafil. Sildenafil is a prescription drug and may have serious health risks if used without medical supervision, particularly if the users are also on concurrent nitrate therapy. The interaction between nitrates and sildenafil can result in profound and life-threatening lowering of blood pressure. The use of nitrates is therefore an absolute contraindication for sildenafil users. Consumers who have purchased VIGA or VIGA FOR WOMEN tablets are urged to immediately discontinue their use and to return them to their place of purchase or directly to Health Nutrition (RMA Laboratories).


**WARFARIN & MICONAZOLE**

**Reminder about interaction**

New Zealand. In a Prescriber Update article prescribers and pharmacists in New Zealand have been reminded of the potentially serious interaction between miconazole oral gel (Daktarin oral gel) and warfarin leading to clinically significant elevations in INR. Six cases of an interaction between oral miconazole and warfarin resulting in INR increases have been reported in New Zealand. In four of these cases patients presented with haemarthrosis, haematuria, haemoptysis or epistaxis. INR values ranged from 7.5 to 18 and were > 10 in all patients with bleeding symptoms. The article also highlights reports of the interaction in Australia. There has also been one report of an interaction between topical miconazole cream and warfarin in Australia.

Chlorproguanil hydrochloride/Dapsone (Lapdap)

The Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom has recently approved chorproguanil/dapsone for the treatment of acute uncomplicated *Plasmodium falciparum* infections. It is registered as a once-daily, three-days treatment for use in all age groups (range of body weight 5-88kg). It will be marketed in most African countries by Glaxo-SmitKline (GSK) under the trade name “Lapdap”.

**Reference:**

Nimesulide

The Committee for Proprietary Medicinal Products (CPMP) in the UK has issued a positive opinion for nimesulide (Aulin, Mesulide, Nimed and associated names) that this is a safe and effective non-steroidal anti-inflammatory drug (NSAID). This opinion is based on a 16-months-long evaluation of the safety and the efficacy data for nimesulide by the CPMP that reinforces a favourable benefit/risk profile to the drug. The drug will have a new Summary of Product Characteristics (SPC) harmonising available medical information from all the European countries where the drug is marketed. According to Helsinn Healthcare SA, manufacturer of nimesulide, the occurrence of hepatic reactions with nimesulide is similar to that of any other NSAID. The CPMP review of nimesulide was conducted after the Finnish National Agency for Medicine (NAM) decided to temporarily suspend the drug from the market in March 2002, in reaction to hepatic adverse effects reported in a number of patients treated with the drug (see WHO Pharmaceuticals Newsletter No.4, 2002).

**Reference:**