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This edition focuses on adverse drug reaction reports attributed to the use of analgesics received at the National Pharmacovigilance Centre from September 2004 to August 2008. We have also compiled adverse reaction reports of interest and pharmacovigilance news from other countries. Persons interested in research will find our 'For your information' section particularly useful. Please feel free to give us a feedback, we love hearing from you.

A DESCRIPTION OF ADRS RECEIVED BY THE NPC THAT WERE DUE TO ANALGESICS

S/N	CLASS OF ANALGESICS	TYPE OF ANALGESICS	FREQUENCY	REPORTED ADVERSE DRUG REACTIONS (ADRs)	OUTCOME
1.	Paracetamol	Paracetamol alone Paracetamol in combination with Orphenadrine, Caffeine, dextropropoxyphene and other analgesics like ibuprofen and diclofenac	3 10	Pruritus, hyperpigmented rash, general body discomfort, uncontrollable swelling of neck region, tonque spasm and protrusion, panic attack and acute stooling and GI upset	Hospitalization: 1 Resolved: 8 Recovered with disability: 1 Ongoing: 2 Others: 1
2.	Aspirin		3	Peri-orbital Swelling, pruritus, tinnitus, chest and neck pain, vertigo and sleeplessness	Resolved: 1 Unknown: 2
3.	NSAIDS	a. Diclofenac	25	Haematemesis, Periorbital swelling, Vomiting, GI ulceration, Abdominal discomfort, diarrhea. Itching of extremities, Hypersensitivity reactions, Dyspnea, Palpitation, tinnitus, Dizziness	Unknown: 3 Resolved: 18 Ongoing: 3 Others: 1

		b. Ibuprofen	7	Facial oedema with blurred vision, Tinnitus and hearing imbalance, weakness, dizziness, choking feeling, difficulty in breathing and insomnia	Unknown: 1 Resolved: 3 Recovered with disability: 1 Ongoing: 1 Others: 1(sneezing)
		c. Naproxen	10	Ototoxicity, rash- hyper pigmented rash, weakness and lethargy, dyspepsia, tightness in chest, palpitation, nervousness, sweating & shivering	Resolved: 5 Recovered with disability: 3 Unknown: 2
		d. Nimesulide	9	Uncontrolled twitching, swollen face with headache, neuritis, itching and darkening of skin, sweating, insomnia, frequent urination	Resolved: 7 Recovered with disability: 1 Unknown: 1
		e. Tenoxicam	4	Diarrhea, GI Irritation, itching, darkening and puffiness of the face	Resolved: 2 Unknown: 2
		f. Ketoprofen	2	Ulcer-type Pain and restlessness	On going: 1 Unknown: 1
		g. Piroxicam	1	Shivering and rigor	Resolved: 1
		h. Unknown	2	Upper GI Bleeding	Unknown: 2

4.	Selective CO-X 2 Inhibitors	Celecoxib	3	Bipedal edema, tightening of throat passage, upper GI bleeding	Resolved: 3
5.	Opiod Analgesics	a. Tramadol	10	Vomitting, Drowsiness, Abdominal Discomfort, Nausea, Restlessness, sweating, Ear discomfort and thirst	Resolved: 9 Unknown: 1
		b. Pethidine	2	Nausea and Vomitting	Resolved
		c. Pentazocine	1	Shivering and Rigor	Resolved
6.	Others	REVIVE-GOLDEN SIX	1	Edematous feet	Resolved with disability
		Combination Analgesics	10		
	TOTAL		103		

Some Adverse Drug Reaction Case Reports and Pharmacovigilance News involving commonly used Drugs.

1. Camphor

Status epilepticus in an infant following transcutaneous administration: case report

A 4-month-old girl developed status epilepticus after receiving an abdominal massage with an unlabelled camphor-containing solution [dosage of camphor not stated] due to its anti-flatulence effects.

The girl was admitted to intensive care because of repetitive seizures with bradycardia and apnoea. One week earlier, she had been hospitalized with vomiting and abdominal distension. During a flight to Paris, she had a generalized eyelid myoclonus. At the airport, she had a generalized convulsion and received diazepam intrarectally.

In the Neurology Department, the girl experienced a series of generalized tonic-clonic seizures followed by status epilepticus, despite receiving phenytoin and clonazepam. Her seizures responded to clonazepam 0.4 mg/kg/day and Phenobarbital. An EEG revealed a generalized convulsion and a slowed rhythm. Following further questioning, her parents revealed that the nanny had massaged the child with a solution thought to have anti-flatulence effects, 72 hours before the onset of seizures; toxicological analysis confirmed the presence of camphor. After 3 days, the girl was extubated. Her neurological status improved within a week and was normal at discharge.

Author comment: *"the development of seizures 72h after abdominal massage suggests delayed absorption of camphor via the transcutaneous route."*

Guilbert J, Flamant C, Hallalel F, Doummar D, Frata A, Renolleau S. Antiflatulence treatment and status epilepticus: a case of camphor intoxication. Emergency Medicine Journal 24: 859-860, No. 12, 1 Dec 2007 - France

Culled from Reaction Weekly 5 April 2008 Edition No. 1196

2. MHRA warning about cough and cold medicines in under twos

The UK Commission on Human Medicines (CHM) has announced that certain medicines should no longer be used in children under the age of 2 years, advises the MHRA.

The MHRA say that the cough and cold medicines which will no longer be licensed for children under the age of 2 years contain the following ingredients:

- Brompheniramine, chlorphenamine and diphenhydramine
- Dextromethorphan and pholcodine
- Guaifenesin and ipecac

- Phenylephrine, pseudoephedrine, ephedrine, oxymetazoline and xylometazoline.

The MHRA advises that the following products, which contain the above mentioned ingredients, should be removed from open shelves: Asda Children's Chesty Cough Syrup; Boots Chesty Cough Syrup 1 Year Plus; Boots Sore Throat and Cough Linctus 1 Year Plus; Buttercup Infant Cough Syrup; CalCough Chesty; and Children's Chesty Cough. The MHRA notes that these medicines can still be supplied under the supervision of a pharmacist for older children. It says that the pharmaceutical industry has voluntarily agreed to change the labels of the affected products to remove dosage instructions for children aged under 2, and to add additional instructions for children aged 2-6. the MHRA advises that coughs and colds in children aged < 2 years should be managed with ibuprofen or paracetamol, together with simple cough mixtures.

MHRA. Updated advice – Over-the-counter cough and cold medicines for young children. Media Release: 27 Mar 2008. available from: URL: <http://www.mhra.gov.uk>

Culled from Reaction Weekly 5 April 2008 Edition No. 1196

3. Antimalarials increase neutropenia risk in HIV-infected children

Malarial treatment with artesunate plus amodiaquine increases the risk of neutropenia in HIV-infected children, according to results from a study conducted in Uganda.

Data were analyzed from 26 HIV-infected children who received a total of 35 treatments for malaria and 134 HIV-uninfected children who received a total of 258 treatments. Malarial treatment consisted of amodiaquine 10 mg/kg for the first 2 days, followed by 5mg/kg on day 3, and artesunate 4 mg/kg for 3 days.

Artesunate plus amodiaquine was an effective treatment for malaria in both the HIV-infected and HIV-uninfected cohorts. However, the risk of neutropenia occurring 14 days after treatment initiation was significantly higher in the HIV-infected cohort, compared with the HIV-uninfected cohort (45% vs 6%; $p < 0.001$). Compared with HIV-uninfected children, HIV-infected children who received artesunate plus amodiaquine had > 7 time the odds of neutropenia of mild severity or greater, and > 24 times the odds of neutropenia of moderate severity or greater. Among HIV-infected children, the risk of neutropenia was significantly higher in those who were receiving antiretrovirals, compared with those who were not (odds ratio 2.3; 95% CI 1.4, 3.6; $p = 0.001$).

In an accompanying editorial, Dr Piero Olliaro, from the UNICEF/UNDP/World Bank/WHO Special Program on Research and Training in Tropical Diseases, Geneva, Switzerland, questioned whether these drugs are unsuitable for patients with HIV. He stated that "before reaching this conclusion, we need to understand what determines the toxicity and which other antimalarial options are safe".

1. *Gasasira AF, et al. High risk of neutropenia in HIV-infected children following treatment with artesunate plus amodiaquine for uncomplicated malaria in Uganda. Clinical Infectious Diseases 46: 985-991, No. 7, 1 Apr 2008.*

2. Olliaro P. Disease and drug interactions : treating malaria with artesunate plus amodiaquine in patients also receiving treatment for concomitant HIV infection. *Clinical Infectious Diseases* 46: 992-993, No. 7, 1 Apr 2008.

Culled from Reaction Weekly 12 April 2008 Edition No. 1197

4. Fluoroquinolones: strengthened warnings requested by FDA

The US FDA has requested the manufacturers of fluoroquinolones to add a boxed warning in the product labelling regarding the increased risk of tendinitis and tendon rupture¹. Exercising its new authority under the food and drug administration amendments act of 2007, the agency has notified the manufacturers of fluoroquinolones to develop a medication guide for the patients, which would be an element under a Risk Evaluation and Mitigation Strategy².

A new analysis by the FDA of the available literature and postmarketing adverse event reports confirmed that fluoroquinolone use is associated with an increased risk of tendon rupture. Furthermore, the risk appears to be increased in patients aged > 60 years, in renal, heart and lung transplant recipients, and in corticosteroid recipients. The FDA has advised healthcare professionals to discontinue fluoroquinolones if the patient develops pain or inflammation in a tendon, to consider potential benefit and risks for each individual patient before fluoroquinolone initiation, and to use fluoroquinolones only for treatment and prevention of infections that are strongly suspected to be caused by bacteria³.

Culled from Reaction Weekly 12 July 2008 No. 1210

¹ FDA. FDA Requests Boxed Warnings on fluoroquinolone Antimicrobial Drugs. Media Release: 8 July 2008. Available from URL <http://www.fda.gov>

² Ibid 1

³ FDA. Fluoroquinolone antimicrobial drugs (marketed as cipro and generic ciprofloxacin) ciprofloxacin extended release (marketed as Cipro XR and Proquin XR), gemifloxacin (marketed as Factive), levofloxacin (marketed as Avelox), norfloxacin (marketed as Noroxin) and ofloxacin (marketed as floxin and generic ofloxacin) Internet Document: {4 pages}, 8 July 2008. Available from URL: <http://www.fda.gov>

FOR YOUR INFORMATION !!!

Patient Safety Research Grants-Better Knowledge for Safer Care

The WHO World Alliance for Patient Safety is offering grants for small research projects dealing with issues of patient safety, including developing or testing local intervention to improve patient safety and cost effectiveness of risk-reducing strategies. The call for proposals opened on 1st July and will close on 30th September. Studies should start in 2009. Sums ranging from \$10,000 to \$25,000 will be available, and proposals are being particularly encouraged. The program concentrates its efforts in four specific areas:

- Global research priorities
- Methods and measures
- Strengthening capacity
- Country research studies

To find out more please go to: <http://www.who.int/patientsafety/research/en/>

ALERT NOTICES !!!

RECALL OF HEPARIN

The Attention of the National Agency for Food and Drug Administration and Control (NAFDAC) has been drawn to the international recall of **Heparin** drug, an anticoagulant used for the prevention of blood clots.

This recall was as result of contamination of the Active Pharmaceutical Ingredient (API) sourced from Changzou Scientific Protein Laboratories (SPL) Changzou, China as well as API from Scientific Protein Labs, Waunakee, Wisconsin US. This has resulted in severe Adverse Reactions and Death.

The implicated Heparin brands are Heparin distributed by **Baxter International Incorporated US** and Heparin-Rotexmedica manufactured by **Rotexmedica GmbH Arzneimittelwerk, Germany, batches 70448, 70587, 70699, 70030, 70056, 70136, 70276, 70097, and 70279.**

NAFDAC hereby alerts healthcare practitioners and the general public to watch out for all brands of heparin from the above mentioned companies particularly the batches of heparin mentioned above. Also healthcare practitioners are to further report any adverse drug reaction observed while using any brand of Heparin.

Similarly, all prescribers and retail outlets are advised to submit any suspected brand of Heparin to the nearest NAFDAC office.

For further enquiry, please contact the National Pharmacovigilance Centre NAFDAC Head quarters Abuja on the following numbers:

095241108
096702823
08086899571

Or e-mail us at nafdac_npc@yahoo.com

Warning Against the use of "Viamax Energizer"

The attention of the National Agency for Food and Drug Administration and Control (NAFDAC) has been drawn to a recent warning by Danish Medicine Agency on the product "Viamax Energizer" which is sold on the internet as a product providing energy. Analysis of this product has shown that it contains levodopa and theophylline contrary to the manufacturer's claim that the drug is a well blended natural herbal product.

Levodopa and theophylline are used in the management of Parkinson's disease and in the treatment of asthma respectively. Due to the associated side effects of these drugs, their use requires competent medical supervision and should therefore not be taken without prescription.

Consequently, NAFDAC hereby warns the general public against the use of Viamax Energizer which has the potential of causing harm to the user.

Viamax Energizer is not a NAFDAC registered product and should not be offered for sale or use in Nigeria.

NAFDAC advises the public to patronize only NAFDAC registered products to be assured of their quality, efficacy and safety.

PHARMACOVIGILANCE/FDIC NEWS : A MONTHLY NEWSLETTER OF NATIONAL PHARMACOVIGILANCE CENTRE(NPC).

NATIONAL AGENCY FOR FOOD AND DRUG ADMINISTRATION AND CONTROL (NAFDAC) PLOT 2032 OLUSEGUN OBASANJO WAY, WUSE ZONE 7, ABUJA, PMB 5032 Wuse Abuja

Telephones: +234-(0)9-6702823;

Fax: +234-(0)9-5241108

E-mail: nafdac_npc@yahoo.com

Web Site <http://www.nafdacnigeria.org/pharmacovigilance.htm>