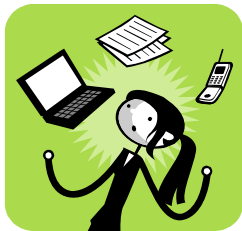




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Keep up to date with the safety of marketed medicines! The mission of the EU Pharmacovigilance Working Party (PhVWP) is to provide recommendations to the EU scientific committee (CHMP) of the European Medicines Agency (EMA) on all matters relating directly or indirectly to "pharmacovigilance" i.e. the constant monitoring of marketed medicines. This includes provision of advice on the general safety of medicines and specifically on the investigation of adverse drug reactions associated with marketed medicines in the EU; this enables the CHMP to effectively manage risk at any phase in the lifecycle of a medicine. Since September 2009, it has published a monthly meeting report of its safety discussions on the EMA website (<http://www.ema.europa.eu/htms/human/phv/reports.htm>). These reports provide an important insight to evolving safety issues with specific medicines. The IMB plays an active role in the activities of the PhVWP, and safety recommendations are implemented by the IMB at national level as appropriate. [Editor's note: These reports are useful for keeping prescribers up to date with potential / evolving problems. The safety issues below serve as an example of the type of information that was made available in recent meeting reports.]



Evaluating the risk of VTE with oral contraceptives. Venous thromboembolism (VTE) is a well-known but rare adverse reaction of oestrogen- and progestogen-containing contraceptives (COCs). The PhVWP recently reviewed 2 observational studies that assessed the risk of VTE in current users of different types of COCs (*see Therapeutics Today Oct 2009 for study details*). The results of these studies confirmed that the risk of VTE for COCs containing low dose ethinylestradiol (EE) and levonorgestrel ("second generation pills") is about 20 cases/100,000 woman-years of COC use, and about 40/100,000 woman-years for COCs containing EE in combination with either desogestrel or gestodene ("third generation pills"). This compares with a risk of 5 cases/100,000 woman-years with no COC usage and 50/100,000 during pregnancy. The PhVWP has noted that these studies suggest that the risk of VTE with the COCs combining EE with drospirenone (Yasmin®) might be higher than previously estimated, lying between the risk of second and third generation COCs. The group concluded that the Summary of Product Characteristics (SmPC) of EE-drospirenone COCs should be amended to include this safety information. [Editor's note: further background information available at: www.ffprhc.org.uk]



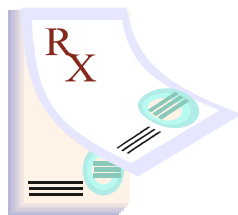
Fluoxetine: risk of cardiovascular birth defects. A study, published in 2008 suggested a possible causal association between cardiovascular (CVS) birth defects and the use of fluoxetine during the first 3 months of pregnancy (*BJCP 2008; 66: 695-705*). The PhVWP requested that the original licence holder for fluoxetine should conduct a systematic critical meta-analysis (n= 9 studies) of all available epidemiological data regarding the effects of first trimester fluoxetine exposure and the risk of congenital malformations with a particular focus on cardiac defects. Following evaluation of this meta-analysis, the PhVWP has concluded that the risk of having an infant with a cardiac defect following use of fluoxetine during the first trimester is increased to approximately 2/100 compared with an expected rate of such birth defects of about 1/100 in the general population. The PhVWP also considered that the small increase in risk of CVS congenital malformations must be weighed against the risks of untreated depression during pregnancy. It has been recommended that the Summary of Product Characteristics (SmPC) for all fluoxetine-containing products should be updated in section 4.6 to reflect this new information; the patient information leaflet will also notify users to talk to their doctor as soon as possible if they become pregnant / are planning to become pregnant while taking fluoxetine. [Editor's note: further background information is available in the Feb report of the PhVWP (web address as above) and on the IMB website www.imb.ie. The NMIC is happy to deal with enquiries regarding choice of anti-depressant during pregnancy - just contact us!]



New rules on epilepsy and driving. Driving is often an emotive issue for patients after they have had a seizure because driving prohibitions may impact on a patients' social and economic status. A recent paper discussed new EU epilepsy and driving requirements, due to be implemented in Ireland and other EU member states in August 2010 (*IMJ 2010; 103:86-88*). Epilepsy is a disorder of the brain characterised by an enduring predisposition to generate unprovoked seizures. Diagnosis is very much based on the clinical history as well as further investigations including neuroimaging and electroencephalography (EEG) which may or may not demonstrate an underlying abnormality. **Currently in Ireland**, a person with epilepsy or an unprovoked seizure can drive small / personal vehicles if they are one year seizure-free. Patients with epilepsy or with a history of a single unprovoked seizure are not allowed to drive larger / commercial vehicles such as lorries, buses or heavy goods vehicles. There are special rules pertaining to specific groups such as those with purely nocturnal seizures, those with simple partial seizures and those with "provoked" seizures (e.g. occurring during an acute encephalitis). **The new EU legislation** attempts to unify existing member state legislature on medical conditions (including epilepsy) and driving. It divides vehicles into 2 main categories: group 1 consists of small/personal vehicles (i.e. up to 3.5 tonnes) and group 2 consists of large/heavy goods vehicles, passenger-carrying vehicles over 3.5 tonnes and those with ≥ 9 seats. While many recommendations are similar to those currently in force, the new rules attempt to clarify issues such as driving during withdrawal of anti-epileptic drugs (AEDs), structural brain lesions and post-epilepsy surgery as follows:

- Where AEDs are being withdrawn, patients should be advised not to drive from the commencement of the period of withdrawal and thereafter for a period of 6 months after cessation of treatment. If seizures occur while withdrawing from the medication, the patients may drive 3 months after reinstatement of AEDs
- Patients post epilepsy surgery may drive after one year of seizure freedom
- Patients with a structural intra-cerebral lesion / certain disorders (e.g. AV malformation or intra-cerebral haemorrhage) with an increased risk of seizures, even if seizures haven't yet occurred can only be certified to drive if the risk of seizures is felt to be $\leq 2\%$ per annum

In addition, patients with epilepsy who achieve 10 years of seizure and medication freedom may be able to drive group 2 vehicles. For a full description, check out the Commission Directive, available online at http://eur-lex.europa.eu/RECH_reference_pub.do (Official Journal of the European Union 26th August 2009). **Readers are also recommended to download this IMJ paper from March of this year (www.imj.ie) as it gives a clear and concise summary of the new legislative provisions.**



How to avoid prescribing errors. It is estimated that 7.5% of prescriptions in general practice contain an error (although probably $<1\%$ contain errors likely to harm the patient). A recent paper reviewed avoidable prescribing errors (*Prescriber 2010; 21:52-55*). Whether prescribing errors result in harm to patients depends on a number of factors. **Firstly** certain patients are at particularly high risk, including older, frail patients, those with several co-morbidities taking several medicines concomitantly, those with acute medical problems and those that are ambivalent about taking their medicines or have cognitive problems. It is particularly important to ensure that such patients and/or their carers are shown how to take medication correctly and to adjust the type of medicines used accordingly. **Secondly**, studies have shown that **4 classes of medicines (anti-thrombotics, anticoagulants, NSAIDs, diuretics) are associated with about 50% of drug-related hospital admissions**, therefore special care is needed when prescribing these medicines. Other drugs include those with a narrow therapeutic index (e.g. methotrexate, digoxin, amiodarone). The author advises prescribers to ensure that they have all necessary information about (a) the patient (such as disease / allergy status and existing medication(s)) and (b) the medicine to be prescribed, available to them before writing a prescription and recommends that they should have dosing calculations checked wherever possible.