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The Final Word on COX-2 inhibitors – for now! The European Medicines Agency (EMEA) has completed its current review of the COX-2 inhibitor (COX-2-Is) class of drugs (www.emea.eu.int). It has concluded that the **risk of serious and potentially fatal skin reactions, associated with Valdecoxib (Bextra®) outweighs its benefit and therefore the drug will remain suspended for a year,** after which time any further safety or other relevant data, submitted by the company will be re-evaluated. The EMEA has repeated its previous recommendations for use of the remaining COX-2-Is still on the market, (celecoxib, etoricoxib, parecoxib):

- COX-2-Is should not be used in patients with established heart disease and/or stroke or in patients with peripheral arterial disease.
- They should be used with caution in patients with risk factors for cardiovascular disease (CVD) e.g. hypertension, hyperlipidaemia, diabetes, smoking.
- They should be prescribed at the lowest effective dose for the shortest duration possible in view of the association between CVD risk and exposure to COX-2-Is,

Prescribers are also reminded that hypersensitivity reactions, and rare, but serious and sometimes fatal, skin reactions can occur with all COX-2-Is, usually in the first month of use and possibly more likely to occur in those with a history of drug allergy.

HRT and Endometrial Cancer. It is well accepted that use of oestrogen-only hormone replacement therapy (oeHRT) increases the risk of endometrial cancer. To counteract this effect, postmenopausal (PM) women with an intact uterus are usually prescribed combined HRT containing progestogens and oestrogens (cHRT). The relationship between the various HRT types and the incidence of endometrial cancer was recently reported from the UK Million Women Study. ***(Lancet 2005; 365: 1543-51).*** In the study 45% of 716,738 PM women (n=320,953) were taking some type of HRT on recruitment. Of these, 45% were using sequential cHRT, 22% continuous cHRT, 9% tibolone and 4% oeHRT (HRT type unknown in remainder). During a follow-up of an average 3.4 years, 1,320 new endometrial cancers were diagnosed in the study group. Compared with never users of HRT, an increased risk for endometrial cancer was noted with tibolone (79% increase) and oeHRT users (45% increase). In comparison, use of sequential cHRT had no apparent effect, while continuous cHRT reduced the risk by 29%. Body mass index (known to be a risk factor for endometrial cancer) affected these results so that the maximum benefits for continuous cHRT were noted in non-obese women and the maximum adverse outcomes for tibolone and oeHRT were greatest in non-obese women. There were insufficient data to provide reliable estimates of the incidence of endometrial cancer after use of HRT ceases. The authors remind readers that a previous report from this study showed that cHRT preparations were associated with a 2-fold increased incidence of breast cancer compared with non-HRT users ***(Lancet 2003; 362: 419-27).*** [Editor's note: Since breast cancer is commoner, the apparently favourable findings for endometrial cancer with continuous cHRT are far outweighed by risk for breast cancer with use]

Medical Students in Primary Care. Ever wondered what patients think of medical students who join your surgery as part of their medical training? A study (BMJ 2005; doi:1136/bmj.38492.599606.8F) was carried out recently in five general practices in the UK, involved in medical student training. The students were part of a graduate-entry medical school course where patients in primary care are seen in either teaching consultations (usually 2 students taking a history with / without undertaking a supervised medical examination) or in "prearranged" consultations used primarily for teaching purposes. In all cases, patients' consent was sought and obtained prior to student contact. Patients with and without student contact completed standard questionnaires [Patient Enablement Index (PEI), Consultation Satisfaction Questionnaire (CSQ)]; in addition, some patients took part in focus group discussions. Of the 487 patients who completed the questionnaires, there was no difference in PEI or CSQ ratings between the test and controls groups. Results from the focus groups showed that overall, patients reported more advantages than disadvantages of participating in the student teaching. However, their willingness to participate was conditional and influenced by factors such as the nature of their condition (and possible type of examination) the number, age and sex of the students. Of interest, while patients accepted that student involvement was part of hospital care, such interaction was viewed differently in the primary care setting. Patients with chronic conditions expressed a worry that such teaching might interfere with the continuity of care from their specific GP. The authors recommend that GPs involved in training should be aware of the need to provide their patients with sufficient information to enable them to give informed consent.

Eye *drops not needed for infective conjunctivitis!* Conjunctivitis is a common condition in childhood. Controversy exists over whether pharmacological treatment is necessary in all cases. A randomised control trial ***(PJ 2005; 274: 781)*** was recently carried out at primary care level in 326 children (6 months – 12 years) with a clinical diagnosis of conjunctivitis. Subjects were randomised to receive either chloramphenicol 0.5% eye drops or placebo drops. The drops were instilled in the affected eye every 2 hours for 24 hours, then 4 times /day until 48 hours after symptoms resolved. Results showed that 86% of treated children achieved clinical cure (no symptoms at day 7) compared with 83% in the placebo group. The mean difference in time to clinical cure was 0.2 days and while bacterial eradication was higher in the treated versus placebo groups (40% vs. 23%), relapse rate at 6 weeks was < 5% overall with no difference between the groups. The authors state that the time gained with active treatment has to be weighed against the personal and health care costs of a condition that improves without treatment in most cases.

Statins and the risk of colorectal cancer. Colorectal cancer (CCA) is a major cause of mortality and morbidity in the developed world. A recent study ***(NEJM 2005; 352: 2184-92)*** examined the potential effect of statins in reducing the risk of CCA. A population-based case-control study of patients with CCA was used to identify cases (n=1,953) from a defined geographical area in Israel who were matched with controls (n=2,015) from the same area. Information on medication use, health and lifestyle habits (including dietary), medical and family history was gathered from all participants. Results showed that use of statins for ≥ 5 years was commoner in the controls compared with cases (12% (n=234) vs. 6% (n=120) respectively). When this was adjusted for known risk factors, the results showed a 47% reduction in the risk of CCA in statin-treated patients relative to the control group. No protective effect was noted for fibric acid derivatives; however patient numbers were very small. In terms of absolute risk reduction, the authors estimated that for the average-risk Israeli population, 4,814 persons would need to be treated (NNT) with statins to prevent one case of CCA; this NNT would halve for high-risk patients (e.g. those with family history of CCA). [Editor's note: The large NNT does not support the use of statins in the prevention of CCA but the results should help to dispel the suggestion that long-term usage of statins may be associated with increased levels of CCA]

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. *This newsletter is produced by the National Medicines Information Centre and the Trinity College Department of Therapeutics, Trinity Centre, St. James's Hospital, Dublin 8. Tel:Direct Line (01) 473 0589 or 1850 727 727 Fax: (01) 473 0596 Email: nmic@stjames.ie*