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Celebrex (celecoxib) **capsules**

**IMPORTANT NEW SAFETY INFORMATION**
**CARDIOVASCULAR RISK**

21st February 2005

Dear Healthcare Professional

In December 2004, you received safety information about Celebrex (celecoxib) regarding preliminary cardiovascular results from long-term placebo controlled trials. On February 17th 2005 Pfizer following a discussion with the European Medicines Agency (EMEA) and Irish Medicines Board has revised the product labelling with important new Celebrex safety information.

**Summary of the prescribing information and changes are outlined below:**

Celebrex (celecoxib) is indicated for symptomatic relief in the treatment of osteoarthritis and rheumatoid arthritis.

- In osteoarthritis: the recommended daily dose is 200 mg taken once daily or in two divided doses.
- For rheumatoid arthritis: the initial recommended daily dose is 200 mg taken in two divided doses.
- In both indications the dose may be increased to 400 mg per day (in divided doses) if needed. In the absence of increased therapeutic benefit after two weeks, other therapeutic options should be considered.
- In all cases the patient's response to therapy should be re-evaluated periodically. The decision to prescribe celecoxib should be based on an assessment of the individual patient's overall risk. Cardiovascular risks of treatment may increase with dose and duration of exposure, therefore the lowest effective daily dose should be used for the shortest duration possible.

**Celebrex is now CONTRAINDICATED in patients with established ischaemic heart disease or cerebrovascular disease.** In addition Celebrex is now contraindicated in class **II**-IV NYHA congestive heart failure. **Celebrex should not be prescribed to such patients.**

Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) or peripheral arterial disease should only be treated with celecoxib after careful consideration.

Based on new analyses of placebo controlled studies, the frequencies of myocardial infarction, heart failure and aggravated hypertension have been found to be uncommon (≥1/1000, <1/100) and that ischaemic stroke rare (≥1/10,000, <1/1000)

Preliminary safety information from three long-term studies in sporadic adenomatous polyps and Alzheimerís disease with celecoxib is now available. In one of the three studies there was a dose-related increase in cardiovascular events (mainly myocardial infarction, MI) at doses of 200mg BID and 400mg BID compared to placebo. The increased risk persisted throughout the study period (33 months). The relative risk for a composite endpoint of cardiovascular death, MI or stroke was 3.2 (95% CI 1.3 – 8.0) for 400mg BID and 2.5 (95% CI 1.0 – 6.3) for 200mg BID of celecoxib compared to placebo. Preliminary data from the other two long-term studies have not shown significantly increased cardiovascular risk with celecoxib 200mg BID and 400mg QD compared to placebo.

Physicians are advised to consider this new information when evaluating appropriate treatment for their patients.

The Product Information for Celebrex has now been revised accordingly (see attached).

If you have any questions concerning this important safety information, please contact Pfizer Ltd. on freephone 1800 633 363 and ask for Medical Information.

Any suspected adverse drug reactions should be notified to the drug safety group at Pfizer Ltd., UK and the Irish Medicines Board in the usual away. The contact details for Pfizer are Pfizer Ltd., Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK or by using freephone 1800 633 363 and asking for the Drug Safety Group.

Yours Sincerely,

John Farrell.

Dr John Farrell
Medical Director