STUDY RESULTS SHOW COMPARABLE EFFICACY BETWEEN CELECOXIB AND DICLOFENAC FOR THE TREATMENT OF ANKLE SPRAINS

Data Presented at EULAR Annual Congress

Stockholm, Sweden (June 14, 2002) – Results from a study presented today at the European League Against Rheumatism (EULAR) Annual European Congress of Rheumatology, showed that celecoxib was as effective in relieving the acute pain of ankle sprain as the non-specific non-steroidal anti-inflammatory (NSAID) diclofenac.1,2

Celecoxib is authorized for marketing in the European Union (EU) for the treatment of osteoarthritis (OA) and rheumatoid arthritis (RA). The drug has been approved for use in the United States for osteoarthritis, adult rheumatoid arthritis, primary dysmenorrhea (painful menstrual cramping), and the management of acute pain. Celecoxib is approved in 15 countries for the management of various pain indications.

“We designed this trial to compare the effectiveness of celecoxib with diclofenac, a non-specific NSAID commonly prescribed around the world, and found that celecoxib was as effective as diclofenac in treating ankle sprains,”3 said lead investigator Jaime Pedraza Yepes, M.D., Assistant Professor, Department of Orthopedic Surgery, Fundación Santa Fe de Bogotá, Colombia.

Celecoxib and Diclofenac: Study Results Show Comparable Efficacy

In this multicenter, randomized, active-control, double-blind, parallel-group study, 450 patients with first- or second-degree acute ankle sprains incurred within no more than 48 hours were randomized to receive celecoxib 200 mg twice daily (BID) or diclofenac 75 mg BID for seven days.4,5 Pain assessments made at baseline and at the fourth and eighth day showed that celecoxib was
comparable to diclofenac in improving the signs and symptoms of ankle sprains.\textsuperscript{6,7} At the end of the study, the percentage of patients who were able to function normally was similar between the two groups: 59.5 percent of patients treated with celecoxib and 61.7 percent of patients treated with diclofenac.

The standard treatment tool, Patient’s Global Assessment of Ankle Injury, identified patients considered to be “responders,” or those who had responded to treatment.\textsuperscript{8} The percentage of responders at Day 4 was similar between the celecoxib and diclofenac groups (80 percent and 82 percent respectively).\textsuperscript{9,10} At study conclusion, the percentage of responders had also increased similarly: 90 percent of patients who received celecoxib and 93 percent of patients who received diclofenac had responded to treatment.\textsuperscript{11,12}

**Study Design**

At baseline, pain assessments were similar among patients treated with celecoxib and those treated with diclofenac on another standard tool, the Patient’s Assessment of Ankle Pain Visual Analog Scale (VAS) measuring the intensity of pain as experienced by the patient.\textsuperscript{13,14} Mean ages were 34 years for the celecoxib group and 32 years for the diclofenac group; there were an equal number of males and females in both groups.\textsuperscript{15} The majority of injuries were non-sports related, and all occurred within 48 hours of beginning treatment.\textsuperscript{16}

The trial was conducted at 32 centers in Colombia, Mexico, Venezuela and Argentina.\textsuperscript{17} Adults who were diagnosed with first- or second-degree acute ankle sprains were eligible to participate in the trial if the injury was within 48 hours of beginning the study.\textsuperscript{18,19} Patients also were required to demonstrate moderate to severe ankle pain on weight bearing as defined by the standard VAS scale.\textsuperscript{20,21}

**Additional Information**

Celecoxib is contraindicated in pregnancy and in women of childbearing potential unless using an effective method of contraception; breast feeding; hypersensitivity to the active substance or to any of the excipients; known sulphonamide hypersensitivity; patients who have experienced asthma, acute
rhinitis, nasal polyps, angioneurotic oedema, urticaria or other allergic-type reactions after taking acetylsalicylic acid or NSAIDs; active peptic ulceration or gastrointestinal bleeding; inflammatory bowel disease; severe congestive heart failure; severe hepatic disease; patients with estimated creatinine clearance <30 ml/min.

Upper gastrointestinal perforations, ulcers or bleeds (PUBs) have occurred in patients treated with celecoxib. Therefore, caution should be taken in patients with a history of gastrointestinal disease, such as ulceration and inflammatory conditions, or in patients at special risk.

As with other drugs known to inhibit prostaglandin synthesis, fluid retention and oedema have been observed in patients taking celecoxib. Therefore, celecoxib should be used with caution in patients with history of cardiac failure, left ventricular dysfunction or hypertension, and in patients with pre-existing oedema from any other reason, since prostaglandin inhibition may result in deterioration of renal function and fluid retention.

Caution is also required in patients taking diuretic treatment or otherwise at risk of hypovolaemia. Compromised renal or hepatic function and especially cardiac dysfunction are more likely in the elderly, in whom the lowest effective dose should be used, and therefore medically appropriate supervision should be maintained.

Clinical trials with celecoxib have shown renal effects similar to those observed with comparator NSAIDs. In patients on concurrent therapy with warfarin, serious bleeding events have occurred. Caution should be exercised when combining celecoxib with warfarin.

Celecoxib inhibits CYP2D6. Although it is not a strong inhibitor of this enzyme, a dose reduction may be necessary for individually dose-titrated drugs that are metabolised by CYP2D6. Celecoxib may mask fever.

The amount of lactose in each capsule (149.7 mg in the 100 mg capsule; 49.8 mg in the 200 mg capsule) is probably not sufficient to cause specific symptoms of lactose intolerance.
The drug is co-marketed by Pharmacia Corporation and Pfizer Inc. Pharmacia Corporation (NYSE: PHA) is a top-tier global pharmaceutical company with a leading agricultural subsidiary. Pharmacia's innovative medicines and other products save lives and enhance health and wellness. Pharmacia's 59,000 people work together with many diverse stakeholders to bring these benefits to people around the world, and to create new health solutions for the future.

Pfizer Inc (NYSE: PFE) discovers, develops, manufactures and markets leading prescription medicines for humans and animals, and many of the world's best-known consumer products.

This press release contains forward-looking or anticipatory statements about the companies’ business and financial performance plans which are based on the information currently available and the expectations currently deemed reasonable by the companies. However, because these forward-looking statements are subject to many risks, uncertainties and changes over time, including those referenced in the companies’ filings with the U.S. Securities and Exchange Commission, actual results may differ materially from those expressed or implied by these forward-looking statements. The companies undertake no obligation to update any forward-looking statements as a result of new information or future developments.

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17 “A Multicenter, Double-Blind, Randomized, Parallel Group Study to Compare the Efficacy and Tolerability of Celecoxib vs. Diclofenac in Ankle Sprain (SUCCESS-IID),” Study Report Protocol Number: 149-00-02-154, April 11, 2002 p.3.