# Flurbiprofen Study M84121 Synopsis

## Report No. M84121

### 2.0 Synopsis

<table>
<thead>
<tr>
<th>The Boots Company PLC</th>
<th>Individual Study Table Referring to Part of Dossier:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of Study Drug:</td>
<td>Volume:</td>
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<tr>
<td>Flurbiprofen</td>
<td>Page:</td>
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<tr>
<td>Name of Active Ingredient:</td>
<td>(For National Authority Use Only)</td>
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<tr>
<td>Flurbiprofen</td>
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**Title of Study:** Report on an Open Cross-Over Comparison of Flurbiprofen and Naproxen in Juvenile Spondylitis, Definite and Probable

**Investigator:** On file

**Study Sites:** 1 site in the United Kingdom

**Studied Period (Years):** NA

**Phase of Development:** NA

**Objective:** To compare the therapeutic efficacy of flurbiprofen and naproxen paediatric patients with definite or probable juvenile ankylosing spondylitis (AS)

**Methodology:**
Randomised, open-label, cross over study comprising 2, 12-week treatment periods with evaluations after 4 and 12 weeks in each period in out-patients with definite or probable AS

**Number of Subjects (Planned and Analyzed):** 17 enrolled; 16 analyzed

**Diagnosis and Main Criteria for Inclusion:**
Patients enrolled in the study were male and female patients who were 9 to 18 years of age with definite or probable juvenile AS according to the criteria specified.

Definite juvenile AS – onset before age 16 years characterized in 1 of the following ways:

A. Bilateral sacroilitis of AS type associated with 1 or more of the following: limitation of movement of the back (without obvious extraneous cause), compatible changes on spinal radiographs, and iritis;

B. Bilateral sacroilitis of AS type in the absence of any of the features enumerated in A

C. Unilateral sacroilitis of AS type with or without other feature and in the absence of infection.

Probable juvenile AS – boys aged between 10 and 16 years who had predominantly lower limb arthropathy and carried HLA-B27

Patients were excluded for the following reasons: previous serious adverse reaction to non-steroidal anti-inflammatory agent; a history of asthma, peptic ulcer, haemetemeis, or melena; and the presence of other arthritic conditions.

**Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number:**
Flurbiprofen 25 mg/5 mL (banana-flavoured) syrup or 25 mg tablets, orally, 3 mg/kg daily as 3 divided doses
**Duration of Treatment:** 12 weeks on each treatment

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<tr>
<th>Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number:</th>
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<tr>
<td>Naproxen 125 mg/5 mL (pineapple-flavoured) suspension or 250 mg tablets, 10 mg/kg daily in 2 divided doses</td>
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</table>

**Criteria for Evaluation**

**Efficacy:**
Measured at baseline and at each assessment (Weeks 4, 8, 12, and 16): number of joints with soft-tissue swelling; severity of pain (5-point scale where 0 = none and 5 = very severe) at each painful joint; anterior spinal flexion (by modified Schroeber method); and duration of morning stiffness.

At each assessment, the patient's global condition (compared with the previous visit) was assessed using a 5-point scale (1 = much worse and 5 = much better). At the end of the study, patients were asked whether they had a preference for either treatment or whether there was a detectable difference.

**Safety:**
Side effects and clinical laboratory tests including erythrocyte sedimentation rate were collected at each assessment.

**Statistical Methods:**
Results were analysed using Wilcoxon matched-pairs signed-ranks tests using individual patient differences from baseline.

**Summary/Conclusions**

**Efficacy Results:**
For patients analyzed (1 patient withdrew during the first treatment period), 14 were male and 2 were female, with a mean duration of disease of 37.8 months. Both flurbiprofen and naproxen treatments induced an improvement in all variables assessed. Treatment effects were statistically significant only for flurbiprofen on duration of morning stiffness ($P \leq 0.05$), total joint score ($P \leq 0.001$), and patient's assessment of global progress (after 12 weeks compared with 4 weeks; $P \leq 0.05$). No significant differences between treatments were detected for any of the variables assessed. At the end of the study, 6 patients preferred flurbiprofen, and 5 patients preferred naproxen.

**Safety Results:**
Three patients reported side effects while taking flurbiprofen. Two patients reported side effects while taking naproxen, and in 1 of these patients, the severe abdominal pain, vomiting, and headache led to withdrawal from the study. Side effects were typical of non-steroidal anti-inflammatory agents; side effects not leading to discontinuation were mild or moderate. There was no evidence of a treatment effect of either drug on the laboratory variables examined.
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Conclusions:
In this study both flurbiprofen and naproxen induced a clinical improvement in patients with juvenile spondylitis. For both treatments, all the variables assessed were improved, but statistical significance was reached only for the effects of flurbiprofen on duration of morning stiffness, total joint score, and patients' assessments of global progress. No statistically significant differences were detected between the 2 treatments for any of the variables assessed. These results should be interpreted in the light of the size of the study, the nature of the data, and the relatively low power of the statistical tests employed.

Side-effects of the two drugs were similar in incidence, nature, and severity and were typical of non-steroidal anti-inflammatory agents. No treatment effects on laboratory variables were apparent.