

V. Clinical Efficacy

Pivotal clinical trials with ARTHROTEC® (diclofenac Na 50 mg/misoprostol 200 mcg) have included more than 1500 patients in 14 countries, including Australia, Belgium, Brazil, Canada, France, Germany, Greece, Luxembourg, Mexico, Netherlands, Portugal, Switzerland, United Kingdom, and Venezuela. The results of these trials have clearly demonstrated the effectiveness of ARTHROTEC for acute and chronic treatment of the signs and symptoms of rheumatoid arthritis and osteoarthritis.

The clinical advantage of ARTHROTEC is that it is associated with significantly less gastroduodenal damage compared to diclofenac. This advantage was established in clinical trials involving both rheumatoid arthritic and osteoarthritic patients. Further studies have confirmed ARTHROTEC's long-term efficacy in rheumatoid arthritic and osteoarthritic patients. The following summary describes the design and most important findings from these pivotal trials.

Efficacy of ARTHROTEC in treating rheumatoid arthritis

Two multinational clinical trials, both of 12 weeks duration and of similar design were conducted to compare the efficacy of ARTHROTEC with that of diclofenac in treating the signs and symptoms of rheumatoid arthritis. A total of 685 patients were studied; 341 received ARTHROTEC and 344 received diclofenac. Both studies demonstrated clearly that the presence of misoprostol in ARTHROTEC does not alter the antiarthritic efficacy of diclofenac in patients with rheumatoid arthritis.^{106,107}

In the first study, 36 investigators from eight countries enrolled 346 patients with rheumatoid arthritis.^{1,106} The patient entry criteria included: active rheumatoid arthritis, history of rheumatoid arthritis of at least 6 months' duration; functional grade of I to III (functional capacity classification); symptoms adequately controlled by diclofenac (50 mg b.i.d. or t.i.d.) for at least 30 days prior to the start of the study.^{1,106} Among the exclusion criteria were: arthritis other than adult rheumatoid arthritis, active GI disease, renal or hepatic disease or malignancy, chronic analgesics, or NSAIDs other than diclofenac.

Patients were randomized to receive either ARTHROTEC or 50 mg diclofenac for 12 weeks; 177 received ARTHROTEC, 169 diclofenac. Physicians were allowed to choose a b.i.d. or t.i.d. dosing regimen to ensure adequate control of the arthritis and to change the regimen as necessary during the trial. The treatment groups were similar for age, gender, and assessments of arthritis.

Primary measures of the arthritic condition included physician assessments of joint tenderness/pain and joint swelling, and physician and patient global assessments of arthritis.^{108,109} Secondary assessments consisted of duration of morning stiffness,¹⁰⁸ erythrocyte sedimentation rate (ESR), and functional capacity classification.¹¹⁰ Since all patients had been adequately controlled with diclofenac prior to the study, efficacy was demonstrated by maintaining control over symptoms.

ARTHROTEC was as effective as diclofenac in controlling symptoms of rheumatoid arthritis

The results of each of these assessments showed ARTHROTEC to be as effective as diclofenac in treating rheumatoid arthritis.^{106,111} Two hundred seventy-seven (277) patients completed the study with all arthritis assessments. By all primary measures, the signs and symptoms of rheumatoid arthritis were the same for both groups. In addition, secondary assessments were consistent with these results. This study demonstrates that ARTHROTEC has equivalent therapeutic efficacy to diclofenac. It also supports the conclusion that the presence of misoprostol in the ARTHROTEC tablet does not reduce the efficacy of diclofenac.