HNP PHARMACEUTICALS

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Title	Equivalence study of a topical diclofenac solution (pennsaid) compared with oral diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial.[see comment].
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Abstract

OBJECTIVE:. To compare the safety and efficacy of a topical diclofenac solution versus oral diclofenac in relieving the symptoms of primary osteoarthritis (OA) of the knee, in a randomized, double-blind, double-dummy equivalence trial. **METHODS:** A total of 622 men and women with radiological evidence of primary knee OA and mild to severe symptoms were randomly assigned to treatment with a topical diclofenac solution plus placebo oral capsules, or placebo topical solution plus oral diclofenac (50 mg) capsules. Patients applied 50 drops of study solution and took 1 study capsule 3 times daily for 12 weeks. Efficacy variables were pain and physical function, measured by the Western Ontario and McMaster Universities (WOMAC) VA 3.1 OA Index, and patient global assessment (PGA). Equivalence in the per-protocol group was based on previously defined ranges of clinically significant difference. Safety was assessed by evaluation of adverse events, vital signs, and laboratory data. **RESULTS:** The difference in mean (95% CI) change scores (final minus baseline) between treatments was 13.3 mm (-8.6 to 35.2) for pain (total scale 500 mm), 71.0 mm (-2.4 to 144.5) for physical function (total scale 1700 mm), and 4.3 mm (-1.2 to 9.8) for PGA (total scale 100 mm). The CI for each efficacy variable fell within the predefined equivalence ranges (pain, +/- 75 mm; physical function, +/- 255 mm; PGA, +/- 20 mm), indicating that no clinically relevant difference was found between the 2 treatment arms. Safety analyses of patients applying topical diclofenac solution revealed some minor skin irritation at the application site--mostly skin dryness in 83/311 (27%) patients--but a significantly reduced incidence, relative to oral diclofenac, of total and severe gastrointestinal (GI) adverse events, including dyspepsia, abdominal pain, diarrhea, and nausea. The number of patients developing abnormal liver function tests (including clinically significant elevation), hemoglobin, and creatinine clearance was significantly higher in the oral diclofenac group. **CONCLUSION:** Application of this topical diclofenac solution to the knee of patients with OA produced relief of symptoms equivalent to oral diclofenac, with minor local skin irritation, but significantly reduced incidence of diclofenac-related GI complaints and abnormal laboratory values.