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Prescribing decisions should be made based on the approved package insert in the country of prescription

Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NA
		Study Code:	L_9826
Generic drug name:	Thiocolchicoside	**Date:**	30/Oct/2007

Title of the study:	Myoril injection and capsule in the treatment of acute low back pain (MYLOBAC)		
Investigator(s):	Dr. S. V. Vaidya, Dr. Jyotsna Oak, Dr. Sanjay Dhar, Dr. Parag Sancheti, Dr. Hemant Kalyan, Dr. Rajagopalan, Dr. C. Kamaraj, Dr. S. Rajasekaran, Dr. D. K. Gupta		
Study center(s):	9 centres throughout India		
Study period: Date first patient enrolled: 11/2004 Date last patient completed: 05/2005		**Phase of development:** IV	
Objectives:	To assess two regimens of Myoril injection and capsule in combination with either diclofenac or ibuprofen in patients with acute low back pain		
Methodology:	Type of study: Open-label, non-comparative, multi-centric, Phase IV trial Study schedule: Visit 1 – selection and inititation of treatment Visit 2 – on the 3rd day of treatment Visit 3 – on the 5th to 10th day of treatment		
Number of patients: **Evaluated:**	Planned: 250 Efficacy 171	Randomized: NA Safety: 171	Treated: 183
Diagnosis and criteria for inclusion:	? Adults between 16-70 years of age ? Diagnosis of acute low back pain of recent onset (<48 hours) and defined by ?spontaneous pain intensity at rest > 50 mm of the visual analogue scale (VAS) ? presence of lumbar muscular contracture (evidenced either by palpation or visually) ? Patients admitted to the hospital for treatment of severe low back pain for ≥ 2 days ? Patients who have signed the informed consent form		

Investigational product:	Thiocolchicoside
Dose:	**? Days 1 and 2:** Intramuscular (IM) injection containing 4 mg of Thiocolchicoside (TCC) Dose: One injection b.i.d. (8 mg daily) **? Days 3 to 10:** Capsules containing 4 mg of TCC Dose: Two capsules b.i.d. (16 mg daily)
Administration:	IM injection (Days 1 and 2) & Oral (Days 3 to 10)
Duration of treatment: 5-10 days	**Duration of observation:** 5-10 days
Reference therapy:	Diclofenac or Ibuprofen (Each investigator prescribed either of the two NSAIDs i.e., diclofenac or ibuprofen along with Myoril according to his/her daily practice, but as per the dosage outlined in the protocol.)
Dose:	**Days 1 to 10**: Diclofenac tablet 50 mg b.i.d. OR ibuprofen tablet 400 mg t.i.d.
Administration:	oral
Criteria for evaluation:	
Efficacy:	**Primary criteria**: Pain score by patient-rated VAS **Secondary criteria**: Hand-to-floor distance, Disability Questionnaire (Roland Morris), and physician-rated clinical global impression (CGI) scale
Safety:	Incidence of adverse events
Statistical methods:	**Efficacy:** All the tests were two sided at 5% level. VAS scores were compared to baseline and tested by ANOVA at the end of the study period, with concomitant usage of ibuprofen or diclofenac as a covariate in the statistical model. Within-group changes in hand-to-floor distance and disability questionnaire were tested by Friedman's ANOVA. The CGI scale was evaluated by Fisher's exact test, with usage of diclofenac or ibuprofen as a categorical classification variable. **Safety:** Descriptive analysis

Summary:

Efficacy results:

Primary

? The intensity of spontaneous pain at rest, as measured by VAS, reduced from 67.96+11.16 mm at visit 1 to 42.27+19.02 mm at visit 2 and to 25.78+20.65 mm at visit 3 (Table 11).

Table 11. VAS for the Assessment of Spontaneous Pain at Rest (in mm)

Concomitant Drug		Visit 1	Visit 2	Visit 3
Diclofenac	N	125	125	119
	Mean	68.4	41.9	25.76
	SD	11.53	18.62	20.4
Ibuprofen	N	46	46	39
	Mean	66.78	43.28	25.87
	SD	10.09	20.24	21.65
Total	N	171	171	158
	Mean	67.96	42.27	25.78
	SD	11.16	19.02	20.65

? There was a percent change of 61.12%+2.43% between visit 1 and visit 3, a change that was statistically significant (P<0.0001). The difference in VAS for spontaneous pain between visit 1 (baseline) and visit 2 (percent change = 37.51%+1.97%; P<0.0001) was also statistically significant (Table 12; Figure I).

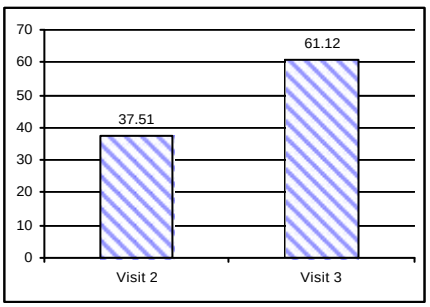
Table 12. Analysis of VAS for the Assessment of Spontaneous Pain at Rest

Variable	**N**	**Mean**	**Std Error**	**Lower 95% CL for Mean**	**Upper 95% CL for Mean**	**Pr > |t|**
vas2diff	171	25.70	1.44	22.85	28.55	<.0001
vas3diff	158	42.14	1.85	38.49	45.78	<.0001
vaspct2	171	37.51	1.97	33.63	41.39	<.0001
vaspct3	158	61.12	2.43	56.32	65.92	<.0001

vas2diff = difference between Visit 1 and 2; vaspct2 = percent change

vas3diff = difference between Visit 1 and 3; vaspct3 = percent change

Figure I. VAS: Percent change in mean value as compared to baseline (Visit 1 –Visit 2 or 3/Visit 1)*100



Efficacy results:	**Secondary** ? At baseline, all patients receiving concomitant ibuprofen and 87.2% of patients receiving concomitant diclofenac were able to bend. At visit 3, more than 97% of patients on diclofenac were able to bend. ? The bending distance between the tip of the hand and the floor decreased at each subsequent visit. This difference in hand-to-floor bending distance between each subsequent visit was statistically significant (P<0.0001). **?** The Rolland Morris disability score reduced at each subsequent visit. From a mean score of 11.56+3.52 at visit 1, the score reduced to 7.5+3.41 at visit 2 and to 5.17+3.71 at visit 3. This difference in Rolland Morris disability scores between each subsequent visit was statistically significant (P<0.0001). ? Almost 95% of all patients showed some improvement in lumbar muscular spasm at Visit 3. Marked improvement was seen in 38.61% of patients, 41.14% patients had moderate improvement, while 14.56% patients experienced slight improvement. More patients on diclofenac (40.34%) had marked improvement as compared to the ibuprofen group (33.33%), while more patients on ibuprofen had moderate improvement (51.28% vs 37.82%). There was no improvement in 5.06% of all patients, while worsening was seen in 0.63% of patients. **?** Out of 156 patients analysed for CGI, 50 (32.05%) had marked improvement and no side effects, 72 (46.15%) had moderate improvement and no side effects and 18 (11.54%) had minimal improvement with no side effects. More patients on diclofenac (37.61%) had marked improvement as compared to the ibuprofen group (15.38%), while more patients on ibuprofen had moderate improvement (58.97% vs 41.88%) and no side effects. There was no improvement in 3.21% of all patients.
Safety results:	? Out of the 171 patients included in the safety analysis, AEs were reported by 9 patients (5.26%). The most frequently reported AE was gastrointestinal disturbance (6 cases; 3.5%). A case (0.6%) of skin eruption was reported, while in 2 cases, the AE was not described. ? Among the 9 patients having presented at least one emergent AE, 3 patients out of 171 (1.75%) reported the event on Day 3 (Visit 2) after the first treatment, and 6 patients out of 158 (3.8%) at Day 5 to 10 (Visit 3). ? No death was reported in included patients. ? No SAE was reported in included patients. ? Overall, AEs in 2 patients (1.1% of the total population) led to study withdrawal. The events were skin eruption and elevation in ASAT and ALAT levels, respectively.
Date of report:	April 1st, 2006