

# ENKORTEN<sup>®</sup> and Relaps Rates in Multiple Sclerosis

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## Enkorten<sup>®</sup>

Enkorten<sup>®</sup> is combination of two neuropeptides that participate in modulation of immunological processes:

- 1-5 adendorphin (acetate).....5 mg
- ACTH 1-13 (acetate) (alpha 1-13 corticotropin).....1 mg

ACTH 1-13 can act: 1) directly on peripheral inflammatory cells, 2) via CNS melanocortin receptors to inhibit inflammation in the periphery and 3) via local receptors on glia to inhibit inflammation within the brain<sup>1</sup>. ACTH 1-13 main mode of action is prevention of NF-κB activation resulting in down regulation of the production of proinflammatory and immunomodulating cytokines (IL-1, IL-6, THF-α, IL-2, IFN-γ, IL-4, IL-13)<sup>2</sup>.

1-5 adendorphin exerts its action through binding to the δ opioid receptors that are located on the neuronal cells and the cells of the immune system. Binding to the neuronal cells δ opioid receptors result in inhibition of neuronal excitability, decrease in neuronal firing rate and inhibition of neurotransmitter release<sup>3</sup>.

## Objectives

Objectives of the study were to determine influence of Enkorten<sup>®</sup> in patients with relapse-remitting (RR) form of MS on relaps rate parameters:

- mean number of relapses,
- relaps duration,
- relapse-free time.

The clinical phase II was carried out between Nov 2005 - May 2007 at the Clinic of Neurology, Clinical Center, University of Sarajevo, Bosnia and Herzegovina. The study was an open, prospective and comparative study lasting for 12 months.

## Patients

- Suffering from RR-MS
  - 25 patients received Enkorten<sup>®</sup>
  - 26 patients in control group
- EDSS (Expanded Disability Status Score) 0 do 5.5

**Table 1. Demographic details and clinical parameters at baseline in patients suffering from RR-MS**

	Enkorten <sup>®</sup>	Control
Age (yrs)	42.2	40.7
F:M	15:10	21:5
BMI (Body mass index)	24.2	23.4
EDSS	3.5*	2.5
T1 MRI lesion (no)	1.12	0.60
T2 MRI lesion (no)	41.83	33.81

\*p=0.01; Mann-Whitney U Test

## Relapses

Table 2. EDSS, Total number of relapses before the study, relaps rate, duration of relapses and time to first relapse during the study for control and Enkorten<sup>®</sup> group and statistical analysis between the groups

	Control N=26		Enkorten <sup>®</sup> N=25		Control vs. Enkorten <sup>®</sup>		
	Mean	SE	Mean	SE	Mann-Whitney U	Z	p-value
EDSS	2.52	0.22	3.52	0.29	190.0	-2.56	0.010
Total number of relapses before the study	7.15	1.65	7.64	0.84	215.0	-2.08	0.037
Relaps rate during the study	1.04	0.23	0.44	0.15	224.5	-2.11	0.035
Duration of relapses (days)	28.19	6.88	9.04	3.54	215.0	-2.29	0.022

## Enkorten<sup>®</sup> Reduced Number of Relapses

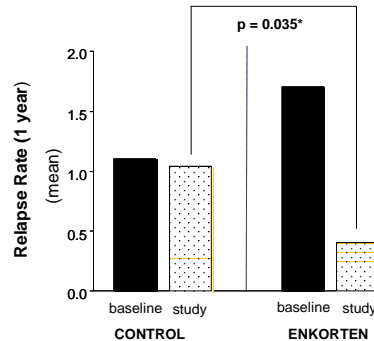


Figure 1. Relapse rate in RR-MS patients at baseline (■) and during 1 year of the study (□) in control (n=26) and experimental group (n=25)

(\*Mann Whitney Test)

### Duration of Relapses

Enkorten<sup>®</sup> Group 9.0 days  
Control group 28.2 days

### Time to First Relapse

Enkorten<sup>®</sup> Group 312 days  
Control Group 238 days

### % Patients without Relapse

Enkorten<sup>®</sup> Group 72.0%  
Control Group 42.3%

## Enkorten<sup>®</sup> Reduced Duration of relapses

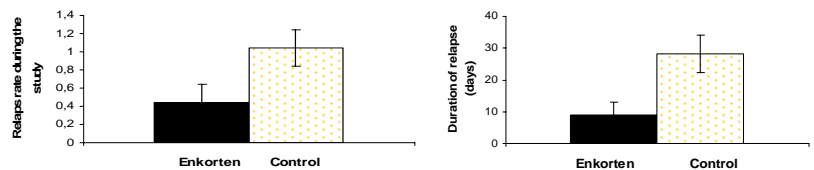


Figure 2. Relaps rate (mean ± SEM) during the study and duration of relapses for control and Enkorten<sup>®</sup> group

(\*Mann Whitney Test)

## Conclusions

**Number of relapses:** Statistically significant reduction in number of relapses was noted in the experimental group compared to control group during the study.

**Duration of relapse:** In addition, duration of relapse state during the study was significantly reduced in experimental compared to control group.

**Time to first relapse:** Cummulative probability of time to first relapse was statistically longer in patients taking Enkorten (experimental group) compared to patients who were free from medication for MS (control group).

**Number of relapse-free patient:** 72% of patients in experimental and 42.3% in the control group remained relapse free throughout the study period of 12 months.

Enkorten<sup>®</sup> was used as a treatment for relapses during the study in the patients from the experimental group. Enkorten<sup>®</sup> has demonstrated its ability as a substitution for corticosteroid pulse therapy during the relapses with significant reduction in duration of these relapses and absence of adverse events that usually accompany corticosteroids. 100% of patients that had relapses of the MS in the experimental group were free from corticosteroids during 12 months of the study.

Enkorten<sup>®</sup> has shown remarkable safety profile with no severe adverse events being reported during 1 year of Enkorten<sup>®</sup> application.

## Literature

- 1) Lipton et al., Ann NY Acad Sci, 1998, 840, 373-380
- 2) Luger et al., Ann NY Acad Sci, 2003, 994, 133-140
- 3) Connor et al., Br. J. Pharmacol. 126, 1999,1553-1558

Sponsor of the project Enkorten<sup>®</sup>-FAR4 was Farmacija d.o.o. Tuzla, BiH  
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