Overview

The only recommended dose of Copaxone (glatiramer acetate) for the treatment of Relapsing-Remitting Multiple Sclerosis (RRMS) is 20 mg injected subcutaneously (SC) daily.

We are aware of two published studies (Fletcher 2002, 1999) that evaluated the safety and efficacy of 20 mg doses of Copaxone when administered daily (QD) or every other day (QOD). Although the second trial (Fletcher 2002) included patients with Relapsing-Progressive MS (RPMS), it should be noted that Copaxone is only FDA-approved for RRMS and not RPMS. The authors of these studies concluded that the QD and QOD treatment groups were equally effective. These studies are summarized below.

- In a published abstract, Flechter (1999) described a small study comparing the safety and efficacy of glatiramer acetate dosed QD vs QOD. In this trial, 58 patients with known RRMS were randomly assigned to receive glatiramer acetate 20 mg QD (n = 20), glatiramer acetate 20 mg QOD (n = 18), or 8 million unit of interferon b-1b QOD (n = 20). Treatment was continued for two years; mean relapse rate per year and mean expanded disability scale score (EDSS) per year were evaluated. The treatment groups were comparable with regard to baseline relapse rate. Treatment results are summarized below.

Copaxone Daily (QD) vs Every Other Day (QD) Dosing in RRMS				
	Relapse Rate (#/year)		**Mean EDSS**	
Treatment Group	**Baseline**	**End Treatment**	**Baseline**	**End Treatment**
Cop 20 mg QD (n = 20)	3.10	1.25*	3.38	3.79
Cop 20 mg QOD (n = 18)	2.94	0.97*	2.44	2.86
Interferon (n = 20)	3.50	1.15*	3.08	3.32
Key: * = significant difference vs baseline (p = 0.0001 in each case) Cop = Copaxone (glatiramer acetate) EDSS = Expanded Disability Scale Score				

  Statistical analyses of differences between groups were not provided. In addition, statistical analyses of changes in EDSS were not provided. The most common adverse events reported with glatiramer acetate were injection site reactions, which appeared to be more frequent with QD vs QOD dosing. In addition, systemic reactions (not defined) were reported with similar frequency in the QD and QOD treatment groups. Premature discontinuation of therapy (reasons not stated) occurred in 2 QD patients and 3 QOD patients. Adverse events associated with interferon therapy included flu-like symptoms, increased spasticity of lower limbs, and systemic reactions. No further information was provided in the brief abstract.

- An open-label, uncontrolled, phase III trial studied the safety and efficacy of QOD Copaxone (20 mg SC) in patients with RRMS (n = 58) or RPMS (n = 10) with a mean age of 35 years and disease duration of seven years (Fletcher 2002). A total of 53 and 41 patients completed one and two years of study, respectively. The mean relapse-rate over two years was reduced 81% from baseline (from 2.9 to 0.56, $p < 0.0001$), a reduction comparable to that seen in a separate, open-label trial of daily Copaxone dosing (see table below). Mean EDSS scores were 2.7 at baseline, 2.71 after one year, and 2.79 after two years of treatment (2.79 vs. 2.72, $p < 0.008$).

The authors reported that results with alternate day therapy were not statistically different from those achieved with daily treatment, aside from a lower dropout rate with alternate day methods. See table below for a comparison of QD and QOD efficacy results.

Copaxone QD vs. QOD Dosing in RRMS and RPMS		
	Copaxone 20 mg SC QOD (n = 68)	**Copaxone 20 mg QD (n = 271)***
Mean disease duration (years)	7	8
Mean annual relapse rate, baseline	1.4	1.4
Mean relapse rate during 2 years of treatment	0.56	0.3
Mean EDSS score, baseline	2.7	3.3
Mean EDSS score, 1st year	2.71	Not available
Mean EDSS score, 2nd year	2.79	Not available
Percent of patients completing 2 years of treatment	60	40
Percent of relapse-free patients at end of 2nd year of treatment (%)	71	54

*Results from a separate, open-label trial

The most common adverse events reported in this trial were injection site reactions (sensitivity, pain, edema, mass, atrophy, inflammation, and hemorrhage) in 61% of patients, immediate post-injection reactions (transient chest pain, palpitations, and tachypnea) in 29%, rash in 7%, and lymphadenopathy in 2%.

Enclosures:

Copaxone Package Insert

References:

Fletcher S, Kott E, Steiner-Birmanns B, et al. Copolymer 1 (glatiramer acetate) in relapsing forms of multiple sclerosis: open multicenter study of alternate-day administration. *Clin Neuropharmacol.* 2002;25(1):11-15.

Flechter S, Vardi J, Rabey JM: Comparison of efficacy between glatiramer acetate and Interferon b-1b in multiple sclerosis patients (MSpts): A two-year follow-up study. *Neurology* 1999 Apr;52(Suppl 2):A497. (Abstract)