

Consistency of symptom improvement in elderly adults with chronic insomnia treated with doxepin 1 mg, 3 mg, and 6 mg

Robert Taylor¹, Joseph Pergolizzi², H Heith Durrence³, Roberta Rogowski³, Thomas Roth⁴

¹NEMA Research Inc, Naples, FL, USA, ²Johns Hopkins University School of Medicine, Baltimore, MD, USA, ³Somaxon Pharmaceuticals, San Diego, CA, USA, ⁴Henry Ford Sleep Disorders Center, Detroit, MI, USA

Purpose

Pain and insomnia are two common health-related complaints. Additionally, the two conditions are often comorbid, with prevalence rates in the literature indicating an overlap of up to 50%. Further, patients with chronic pain and insomnia are often difficult to treat. This report reviews global symptom and severity assessment from two trials evaluating low-dose doxepin (DXP), a selective H₁ antagonist, in elderly adults with insomnia.

Method

Two randomized, double-blind, placebo-controlled trials of doxepin 1 mg, 3 mg, and 6 mg in elderly adults with a DSM-IV-TR definition of primary insomnia were conducted. Study A was a 3-month trial (N=240; DXP 1 mg and 3 mg vs PBO); Study B was a 4-week trial [n=255; DXP 6 mg vs placebo (PBO)]. Symptom improvement was assessed with the two-item Clinical Global Impression scale (CGI), the 5-item Patient Global Impression scale (PGI) and the Insomnia Severity Index (ISI). Selected endpoints are reported corresponding to first (Study A: Day 14; Study B: Day 7) and last assessment points.

Results

DXP 3 mg (Study A; $P < .01$) and 6 mg (Study B; $P < .05$) significantly improved the CGI-Severity and CGI-Improvement scales vs PBO at the first assessment point. At the end of 3 months in Study A, DXP 1 mg and 3 mg significantly improved (all P -values $\leq .01$) both CGI scales vs PBO. After 3 months of treatment in Study A, insomnia symptoms were rated as one category less severe on the CGI by clinicians in both DXP groups compared with PBO (median data). DXP 3 mg (Study A) and 6 mg (Study B) significantly improved the total ISI score at the first and last assessment points vs PBO.

Conclusions

In these two trials, DXP 1 mg, 3 mg, and 6 mg produced significant and clinically meaningful improvements in clinician-rated assessments of illness severity and therapeutic effect and in patient-rated assessments of therapeutic effect, beginning as early as the first assessment point and lasting as long as 3 months. Both patients and clinicians perceived consistent symptom improvement beyond the traditional analyses of quantitative sleep patterns. In summary, the risk/benefit profile of low-dose DXP, a nonscheduled, selective H₁ antagonist with no addiction potential, suggests that it may represent an excellent alternative in the treatment of insomnia in patients with pain conditions.