

Improvement in sleep maintenance and early morning awakenings in adult and elderly patients with insomnia treated with doxepin 3 and 6 mg

Robert Taylor¹, Joseph Pergolizzi², H Heith Durrence³, Brian Dorsey³, Roberta Rogowski¹, Thomas Roth¹

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 the effects of the sleep-specific doses of doxepin (DXP), 3 mg and 6 mg, on sleep maintenance (SM) and early morning awakenings (EMA) in transient and chronic insomnia. Additionally, the safety of these doses is examined in the two pivotal long-term trials.

Method

SM and EMA endpoints from 4 trials are reported. In 3 trials, patients meeting DSM-IV-TR criteria for insomnia were randomized for treatment. Study A was a 12-week (WK) trial of elderly patients [N=240; DXP 3 mg vs placebo (PBO)]. Study B was a 5-WK trial of adults patients (N=221; DXP 3 mg and 6 mg vs PBO). Study C was a 4-WK trial (n=255; DXP 6 mg vs PBO). Study D was a single-night trial that simulated transient insomnia in healthy adults (N=565; DXP 6 mg vs PBO). The primary method of evaluating efficacy was polysomnography (PSG) in Studies A, B, and D, and patient reports in Study C. SM endpoints included polysomnographic wake after sleep onset (WASO) and subjective WASO (sWASO). EMA was assessed with PSG Sleep Efficiency % in the last quarter-of-the-night (SE-LQ). Data from the first and final assessment point [Study A=Night (N) 85; Study B=N29; Study C=WK4] of the study are reported.

Results

DXP 3 mg and 6 mg significantly improved WASO on N1 of all 3 trials ($P < .0001$), with improvements vs PBO ranging from 25 (Study B, 3 mg) to 40 minutes (Study D, 6 mg). DXP 3 mg (Study A and B; $P \leq .0008$) and 6 mg (Study B and D; $P < .0001$) significantly improved SE-LQ on N1 of all 3 trials, with improvements vs PBO ranging from 8% (Study B, 3 mg) to 15% (Study A, 3 mg). DXP 6 mg (Study C; $P < .0001$) significantly improved sWASO in WK1, with improvement vs PBO of 23 minutes. The significant improvements in SM and EMA were maintained at the final time point in all studies, excepting SE-LQ on N29 (Study B, 3 mg $P = .07$). There was no significant next-day residual sedation and no reports of anticholinergic effects or memory impairment in either Study A or Study B. Additionally, there was no evidence of respiratory depression, and no evidence of any discontinuation effects or addiction potential. Safety profiles were comparable between groups.

Conclusions

DXP 3 mg and 6 mg demonstrated significant improvements in SM and EMA endpoints that were consistent and were maintained at the final time point for all but one assessment. These data suggest DXP is effective at treating both SM and EMA in both transient and chronic insomnia populations, and in adult and elderly populations. Importantly, these improvements in sleep did not come at the expense of safety. 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.