Dexmedetomidine Orally Dissolving Film for Acute Agitation Associated with Schizophrenia or Bipolar Disorder: SERENITY I and SERENITY II Trials

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Abstract

Episodes of acute agitation associated with psychiatric disorders are often managed in emergency and inpatient settings. These trials evaluated the efficacy, safety, and tolerability of dexmedetomidine orally dissolving film (ODF), an investigational treatment for acute agitation associated with schizophrenia (SERENITY I) or bipolar disorder (SERENITY II). Dexmedetomidine ODF is a highly selective agonist of alpha 2 adrenergic receptors that modulate norepinephrine release from the locus coeruleus. Two randomized, double-blind, placebo-controlled Phase 3 trials in 15 U.S. sites included participants aged 18 to 75 with acute agitation and a DSM-5 diagnosis of schizophrenia or schizoaffective disorder (Serenity I) or bipolar disorder I or II (Serenity II). Agitation was defined as ³14 on the Positive and Negative Syndrome Scale-Excited Component (PEC) at screening and baseline, and ³4 on at least 1 of the 5 PEC items (poor impulse control, tension, hostility, uncooperativeness, and excitement) at baseline. Randomization was 1:1:1 to dexmedetomidine ODF 120 or 180 mcg or matching placebo. All participants self-administered study drugs. For persistent or recurrent agitation after 2 hours, investigators could redose a half-dose. The primary endpoint was changed from baseline in PEC total at 2 hours. The secondary endpoint was the earliest time at which a statistically significant separation from placebo occurred.A total of 380 patients were randomized in each trial (N = 760). All doses of dexmedetomidine ODF met the primary endpoint of change from baseline in PEC at 2 hours vs placebo ($P < .001$). Statistically significant improvement in PEC occurred as early as 20 minutes with the 180 mcg dose in both trials. A second (half-strength) dose was given to 10 (4.0%) participants in the 180 mcg groups, 34 (13.3%) in the 120 mcg groups, and 58 (23.0%) in the placebo groups in Serenity 1 and Serenity 2. There were no drug-related serious or severe TEAEs in either trial. No participant was unarousable by the Agitation and Calmness Evaluation Scale. For dexmedetomidine 180 mcg, 120 mcg, and placebo, the incidence of TEAEs was 37.3%, 39.5%, and 15.1% in Serenity 1 and 35.7%, 34.9%, and 17.5% in Serenity 2. Somnolence was the most common TEAE in both trials (22% Serenity I; 21% Serenity 2). Of 110 somnolence reports, 75% were mild and 25% moderate. In 2 Phase 3 trials, the investigational treatment, dexmedetomidine ODF, effectively treated acute agitation associated with schizophrenia or bipolar disorder, with onset of action as early as 20 minutes at the 180 mcg dose. Both doses of dexmedetomidine ODF produced a calming effect without unarousable sedation. Mild or moderate somnolence was the most common AE. Dexmedetomidine ODF is a selective alpha-2 adrenergic receptor agonist that allows self-administration, making it a potential addition to noninvasive treatments for acute agitation associated with schizophrenia or bipolar disorder.

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Randomized, Double-Blind, Placebo-Controlled, Fixed-Dose Study to Evaluate the Efficacy and Safety of the Amphetamine Extended-Release Tablet in Adults with Attention-Deficit/Hyperactivity Disorder

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Abstract

Background. Attention-deficit/hyperactivity disorder (ADHD) is a neurobehavioral disorder characterized by pervasive impairment in symptoms of inattention, hyperactivity, and impulsivity. Psychopharmacologic treatment is targeted at the management of symptoms of ADHD, and evidence exists that ADHD persists into adulthood. Clinical practice guidelines recommend a combination of behavior therapy and psychostimulant medication for the treatment of ADHD in children, adolescents, and adults. Psychostimulants are often prescribed for ADHD in adults, and amphetamine long has been considered a mainstay of treatment for this population. As adult patients seek relief from ADHD symptoms early in the workday and into the early evening hours, with fewer required doses, extended-release formulations with an early onset of efficacy and an extended duration of effect are considered very desirable. The amphetamine-extended release tablet (AMPH ER TAB) was developed to provide a portable, easy-to-use amphetamine tablet dosage option that can be chewed or swallowed whole.

Objectives. To evaluate the efficacy and safety of an Amphetamine Extended-Release Tablet (AMPH ER TAB) in adults with ADHD aged 18 to 60 years. Methods: In a 5-week forced dose-titration phase, eligible subjects were randomized to either oral

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