AXS-05 (Dextromethorphan/Bupropion): An Innovative Treatment in Clinical Development for Agitation Associated with Alzheimer’s Disease

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Abstract

Alzheimer’s disease agitation

Alzheimer’s disease (AD) is an irreversible, progressive brain disorder that afflicts an estimated 5 million Americans, a number that is anticipated to increase to approximately 16 million by 2050. In addition to cognitive decline, individuals diagnosed with AD typically experience neuropsychiatric symptoms including agitation, aggression, depression, anxiety, sleep disturbances, and hallucinations. These symptoms are associated with decreased functioning, increased caregiver burden, and premorbid neurocognitive impairment. Recently, agitation in AD has been identified as a significant health-care problem, with a high likelihood of its presence and increased risk of death. Specifically, agitation in AD is a significant health-care problem, with a high likelihood of its presence and increased risk of death. Specifically, agitation in AD is associated with mortality rates and decreased quality of life in AD. The presence of agitation in AD is associated with increased healthcare utilization and costs, and an increased risk of institutionalization.

AXS-05 mechanism of action

AXS-05 is a novel, oral, investigational medicine consisting of dextromethorphan (DM) and bupropion (BUP), in late-stage clinical development for agitation associated with Alzheimer’s disease (AD). AXS-05 is a novel combination drug designed to synergize the therapeutic potential of these two active components, resulting in a new class of compound called AXS. AXS-05 is a unique combination of DM and BUP that addresses the dual targets of serotonin and dopamine reuptake inhibition, as well as other behavioral and psychological symptoms associated with AD.

Clinical Development of AXS-05

Pharmacodynamic synergy has been demonstrated between the two components of AXS-05 in Phase I studies. In studies with AD, clinical results with AXS-05 have demonstrated positive results in reducing agitation and improving other behavioral and psychological symptoms associated with AD, including hallucinations, delusions, and agitation.

DM concentrations of AXS-05: Correlation with agitation symptom reduction

DM concentrations of AXS-05 achieved in clinical trials have been shown to correlate with agitation symptom reduction. In a Phase 2 trial, AXS-05 demonstrated a significant reduction in agitation symptoms as measured by the CMAI, with a greater decrease in symptoms observed in the AXS-05 arm compared to placebo.

Conclusion

AXS-05 is a novel, oral, investigational medicine in clinical development for the treatment of agitation associated with AD. Clinical evidence with other agents that share the mechanism of action of AXS-05 supports its potential in the treatment of agitation in AD. AXS-05 has shown promising results in Phase 2/3 clinical trials, with reported K, values for serotonin and dopamine reuptake inhibition or leading to the symptoms of dementia.

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