double-blind AMPH ER TAB 5 mg starting dose or matching placebo, once daily in the morning beginning the day after the Baseline Visit. Subjects were titrated up (5 mg increments) each week. Safety and efficacy assessments were done weekly. After Visit 3, subjects received 20 mg for 14 (3) days before Visit 5 (V5). Subjects who could not tolerate study drugs discontinued. A Permanent Product Measure of Performance (PERMP) placement test was done at Screening or Baseline. At V5, efficacy assessments included the administration of serial PERMPs predose, 0.5, 1, 2, 4, 8, 10, 12, 13, and 14 hours postdose. The primary efficacy endpoint was the mean PERMP-T score across postdose time points during the Visit 5 serial PERMPs. Safety was monitored by AEs assessed at each visit, C-SSRS, vital signs, weight, and assessment of sleep, appetite, mood, and psychotic AEs.

**Results.** The mean postdose PERMP-T score over all postdose time points at V5 was statistically significantly higher in the AMPH ER TAB group vs placebo (302.8 vs 279.6; $P = .0043$). Common adverse events were decreased appetite, insomnia, and dry mouth. The majority of TEAEs were mild to moderate in severity, and no SAEs were reported.

**Conclusion.** The AMPH ER TAB demonstrated efficacy in the treatment of symptoms of ADHD in adults, with an anticipated safety profile.

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# Post Hoc Analysis of the Impact of Lemborexant on Patient-Reported Sleep and Insomnia Severity in Adults with Insomnia and Depression Histories

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**Abstract**

**Introduction.** The dual orexin receptor antagonist lemborexant (LEM) is approved in multiple countries including the United States, Japan, Canada, and Australia for insomnia treatment in adults. In phase 3 study E2006-G000-303 (Study 303; SUNRISE-2; NCT02952820), LEM provided significant benefit vs placebo (PBO) on subjective sleep outcomes over 6 months and was well tolerated. This post hoc analysis evaluated the effect of LEM on sleep outcome measures and insomnia severity as assessed by the Insomnia Severity Index (ISI) over 6 months in subjects with a lifetime history of depression (DepHx subgroup). We performed this analysis as insomnia in DepHx subjects could be a residual symptom of unresolved depression, and therefore, these subjects may respond differently to insomnia treatment.

**Methods.** Study 303 was a randomized, double-blind, 12 months global study in adults (≥18 years) with DSM-5 insomnia disorder. For 6 months (Treatment Period 1), subjects were randomized to PBO or LEM (5 mg [LEM5]; 10 mg [LEM10]). For the next 6 months (Treatment Period 2; not reported), PBO subjects were rerandomized to LEM and LEM subjects continued their original dose. The inclusion criteria allowed for participation of subjects with a lifetime DepHx, concomitant antidepressant medication use and/or mild depression (maximum Beck Depression Inventory II score of 19). Subjects had a baseline ISI total score (ISI-ts) ≥15.

**Results.** The Full Analysis Set comprised 949 subjects, including 112 subjects in the DepHx subgroup (PBO, n = 34; LEM5, n = 39; LEM10, n = 39). Baseline median subjective sleep onset latency (sSOL; minutes) was 52.9, 57.1, and 70.7 for PBO, LEM5, and LEM10, respectively. At 6 months, greater median decreases from baseline in sSOL were observed with LEM5 (−21.7) and LEM10 (−40.1) vs PBO (−12.9). Baseline mean subjective sleep efficiency (sSE; %) was 62.2, 59.2, and 62.4 for PBO, LEM5, and LEM10, respectively. At 6 months, greater mean (SD) increases from baseline in sSE were observed with LEM5 (17.2 [18.3]) and LEM10 (20.9 [19.0]) vs PBO (14.9 [15.4]). Baseline mean subjective wake after sleep onset (sWASO; minutes) was 123.7, 151.0, and 132.6 for PBO, LEM5, and LEM10, respectively. At 6 months, greater mean (SD) decreases from baseline in sWASO were observed with LEM5 (−52.7 [69.2]) and LEM10 (−68.8 [81.9]) vs PBO (−46.7 [69.4]). Mean baseline ISI-ts were 18.6, 19.9, and 19.0 PBO, LEM5, and LEM10, respectively. At 6 months, greater mean (SD) decreases from baseline in ISI-ts were observed with LEM5 (−9.1 [6.8]) and LEM10 (−10.0 [5.9]) vs PBO (−7.9 [5.6]). Treatment-emergent adverse event rates in the DepHx subgroup were similar to those in the overall study population.

**Discussion.** At 6 months, LEM improved patient-reported sleep outcomes and reduced patient-reported insomnia severity in subjects with DepHx. These results suggest that LEM may be a therapeutic option for patients with insomnia and DepHx.

**Funding.** Eisai, Inc.

# Hyponatremia Secondary Treatment with SSRI Antidepressants in Adults and Elderly

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**Abstract**

**Introduction.** Hyponatremia is an electrolyte disorder that can be caused by multiple factors, among which the syndrome of inappropriate antidiuretic hormone secretion (SIAHS) is one of the most frequent causes. Selective serotonin reuptake inhibitors (SSRIs) are the most widely used antidepressant drugs in all age

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groups for efficacy, safety, and adverse effects, although they can cause serious and undesirable side effects.
**Objective.** Report of a series of cases of patients with SIAHS secondary to the use of SSRIs.
**Materials and Methods.** We report 21 cases of patients between 52 and 76 years of age, of both sexes, undergoing treatment for depressive disorder with SSRI antidepressants and anxiolytics, concomitant with other clinical treatments (ACEI, thiazides, and carbamazepine). Biochemical laboratory and electrocardiogram studies were performed prior to the start of treatment.
**Results.** In the first weeks (mean = 2.5) after starting psychopharmacological treatment, hyponatremia (mean = 126 mEq/L) was recorded in 9 symptomatic patients, and Inadequate Antidiuretic Hormone Secretion Syndrome (SIAHS) was diagnosed with referral to Nephrology and Endocrinology. The SSRI was withdrawn, achieving normalization of the biochemical values (plasma and urinary sodium, plasma, and urinary osmolarity), psychotherapy was reinforced until the rotation of another antidepressant. The mean time of suspension of the antidepressant was 7.1 days, the time of disappearance of symptoms after the suspension was 4.3 days and the normalization of biochemical values was 21.68 days. Only one case was severe and 5 required hospitalization.
**Conclusions.** In the cases presented, the SSRI antidepressants were associated with hyponatremia caused by the syndrome of inappropriate antidiuretic hormone secretion. This adverse event was more significant in elderly patients and in those treated with other drugs that cause the disease, such as antineoplastic, diuretic, and antiepileptic drugs, due to synergism between the causative mechanisms.
**Funding.** No funding

**Keywords:** Antidepressants SSRIs; Hyponatremia; Syndrome of inappropriate antidiuretic hormone secretion

# Social Cognition and Behavioral Variant of Frontotemporal Dementia: Evaluative Utility for the Health and Forensic Field

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**Abstract**

**Introduction.** The behavioral variant of frontotemporal dementia presents clinical specificities and difficulties for its early diagnosis in the initial stages due to the overlap of symptoms with other psychiatric pathologies. The delay in diagnosis places the subject in a state of vulnerability because the treatment will not be adequate and the alteration in the psycho-functional capacity can expose him to risks.
**Objective.** The objective of this research was to describe the importance at the forensic and health level of the neuropsychological evaluation of social cognition in people with behavioral variant frontotemporal dementia and to correlate the results with the clinical manifestations of the patients.
**Materials and Methods.** Forty-five patients with behavioral variant frontotemporal dementia were studied with social cognition tests (Reading the Mind in the Eyes and Faux Pas Tests) and staged with standardized scales (CDR [Clinical Dementia Rating], GDS [Global Deterioration Scale], and the FTD-FRS [Frontotemporal Dementia Rating Scale]). The results were analyzed with descriptive and inferential statistical tests and the current ethical-legal requirements were met (requirement of informed consent, reservation of the identity of the participants, compliance with the GCP-Good clinical practice-, ANMAT provision 6677/10 and adherence to the Ethical Principles derived from the Declaration of Helsinki).
**Results.** We found a significant prevalence of alterations in social cognition tests, mainly in Faux Pas Test, from the initial stages of the disease, which were correlated with the clinical stage of the patient.
**Conclusions.** The behavioral variant of frontotemporal dementia is a condition with significant diagnostic complexity in its initial stages that affects decision-making, the type of treatment to be instituted and presents the consequences for the subject and their environment. Early detection with a deep assessment of social tools will provide clinical tools for pharmacological treatment, as well as to know the capacity and safeguard the rights of the subject and implement the necessary support measures. It was confirmed that the alterations in the social cognition tests were correlated with the clinical stage in the FTD-FRS scale and high implication in the results of the Faux Pas Test mainly, and secondarily in the Reading the Mind in the Eyes Test.
**Funding.** No funding

**Keywords:** Behavioral variant frontotemporal dementia; Social cognition; Capacity; Pharmacotherapy

# Efficacy, Tolerability, and Safety of Atypical Antipsychotics in East Asian Ethnicity

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**Abstract**

**Background.** A number of intrinsic (age, gender, physical comorbidities, genetic factors, and ethnicity), and extrinsic factors (diet, concomitant medications, alcohol use, and smoking) influence an individual's response to psychotropic medications. Data suggest that ethnicity may affect medication efficacy, tolerability, and safety through different pharmacokinetics and pharmacodynamics. Asians have been found to have a high frequency of reduced function of CYP2D6 allele (CYP2D6*10), which contributes to the slower metabolism of some medications compared to other

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