# CNS SPECTRUMS®

THE INTERNATIONAL JOURNAL OF NEUROPSYCHIATRIC MEDICINE

#### ORIGINAL RESEARCH

#### Romantic Attachment in Patients with Mood and Anxiety Disorders

D. Marazziti, B. Dell'Osso, M.C. Dell'Osso, G. Consoli, A. Del Debbio, F. Mungai, L. Vivarelli, F. Albanese, A. Piccinni, P. Rucci, and L. Dell'Osso

Aripiprazole in Juvenile Bipolar Disorder Comorbid with Attention-Deficit/Hyperactivity Disorder: *An Open Clinical Trial* 

S. Tramontina, C.P. Zeni, G.F. Pheula, C.K. de Souza, and L.A. Rohde

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T.J. Oster, C.A. Anderson, C.M. Filley, H.S. Wortzel, and D.B. Arciniegas

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S.M. Stahl

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IN SESSION

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J.A. Lieberman

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A Seven-Year Follow-Up of an Extremely Refractory Bipolar I Patient

BRIEF SUMMARY: Consult the Full Prescribing Information for complete product information

AMPHETAMINES HAVE A HIGH POTENTIAL FOR ABUSE. ADMINISTRATION OF AMPHETAMINES FOR PROLONGED PERIODS OF TIME MAY LEAD TO DRUG DEPENDENCE. PARTICULAR ATTENTION SHOULD BE PRAID TO THE POSSIBILITY OF SUBJECTS OBTAINING AMPHETAMINES FOR NON-THERAPEUTIC USE OR DISTRIBUTION TO OTHERS AND THE DRUGS SHOULD BE PRESCRIBED OR DOSPENSED SAYAMINGY.

MISUSE OF AMPHETAMINE MAY CAUSE SUDDEN DEATH AND SERIOUS CARDIOVASCULAR ADVERSE EVENTS.

IN USER OF AMPHETABINE MAY CAUSE SUDDEN DEATH AND SERIOUS CARDIOVASCULAR ADVERSE EVENTS.

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DISAN-VP criteria for ADVERSE AND SERIOUS CAUSE OF ADVERSE AND SERIOUS CAUSE CITICAL STATES.

A diagnosis of Attention-Delicityhperacitwity Dissource (ADNID, CSM-IVP) implies the presence of hyperactive-impulsive or inattentive symptoms to presence of the presence of impulsion of the company of the serious of the serious of the serious cause clinically significant impairment, in symptoms must cause clinically significant impairment, in symptoms must cause clinically significant timpairment, in symptoms must cause clinically significant impairment, in symptoms must not be better accounted for typ another mental disorder. For the Instendine Type, at least six of the following symptoms must not be better accounted for typ another mental disorder. For the Instendine Type, at least six of the following symptoms must have persisted for at least for months; lack of attention to details/carties symptoms must have persisted for at least for months; lack of attention to details/carties missakes, lack of sustained attention; poor internet following symptoms; lack of sustained attention; the sustained disposition

#### CONTRAINDICATIONS

CONTENDIOLATIONS.
Avanced arientecerises, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, knownyppersensitivity or diosyncasy to the symptomizeric amines, gaucoma. Aplated states.
Patients with a listory of drug abuse.
During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS
Serious Cardiovescular Events
Serious Cardiovescular Events
Serious Cardiovescular Events
Serious Cardiovescular Events
Sudden Death and Pre-existing Structural Cardiac Abnormalities or Other Serious Heart Problems
Children and Adoksconts
Sudden Ideath has been reported in association with CNIS stimulant treatment at usual doses in children and adolescents with structural cardiac ahornmalities or other serious learl problems. Although some serious heart problems alone carry an increased risk in sudden deshit, stimular products generally should not be used in children or adolescents with known serious structural cardioches should not be used in children or adolescents with known serious structural cardioches cardiocrypathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vibinerability to Adoles
Adoles Sudden leathers, stroke, and myocardial intarction base been cardioches.

Adults wilded deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater kielihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rightm abnormalities, conouray rarery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs (see CONTRAINDICATIONS).

cardiac abnormalities, cardium/opathy, sendous nearl reprima anomarines, corolary artery disease, or context serious cardiac problems. Adults with such adhormalities should also generally not be freated with stituted rulary (see CORTARINDICATIONS).
Adults with such adhormalities should also generally not be freated with stituted rulary (see CORTARINDICATIONS).
Simulant metications cause a modest increase in every properties of the properties of the control of the properties of the properties of the control of the properties of the properties of the control of the properties of the properties of the control of the properties of the pro

Beyond assertion assertion in using stimulants to treat ADHD patients, with comorbid bipotar disorder because of concern for prossible induction of mixed manic episode in such patients. Prior to lititating treatment with a stimulant, patients with comorbid prossible induction of mixed manic episode in such patients. Prior to lititating treatment with a stimulant, patients with comorbid prossible in the prior of the pr

short-term, placebo-controlled studies, such symptoms occurred in author to the placebo-treated patients. Aggressive amphiliary to consequence of the placebo-treated patients. Aggressive behavior or hostility is other observed in children and addressorts with ADHO, and has been reported in clinical trials and Aggressive behavior or hostility, better observed in children and addressorts with ADHO, and has been reported in clinical trials and Aggressive behavior in robotility. Descriptions of the placebo-treated patients are supported by the placebo-treated patients and addressorts with ADHO, and has been reported in clinical trials and stimulants cause aggressive behavior in robotility. Descriptions are supported by the placebo-treated proper of the placebo-treated proper over the months of flowith. Careful following possesive behavior in robotility. Long-Term Suppression of Browth.

Long-Term Suppression of Browth

Careful following of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-viseada and non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-viseada and non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-viseada and non-medication treatment groups over 14 months, and the placebo-treatment groups over 14 months and 27 kg less growth in the field at weeks of therapy was 1-11 bs and 2-28 bs, respectively, for patients receiving 10 mg, 50 mg, and 70 mg of adepenatement in children ages 5 to 12 years may

with stimulants, and patients who are not growing or gaming weight as explosed may be an even to have the notation of solutions. There is some clinical evidence that stimulants may lower the convolutive threshold in patients with prior history of seizures, in patients with prior Ec aphormatiles in absence of seizures, and very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

Visual Distribution

Difficulties with accommodation and blurring of vision have been reported with stimulant treatment.

Difficulties with accommodation and blurring of vision have been reported was surround to the commodation and blurring of vision have been reported was surrounded to the commodation of the possibility of overtoosage. Vivanes should be used with caution in patients who use define sympathomimetric drugs.

Ties: Ampletamines have been reported to exacerbate motor and noncit cist and Tourstets syndrome. Therefore, clinical evaluation for its and Tourstets syndrome in children and their families should preced use of stimulant medications, information for Patients: Ampletamines may impair the ability of the patient to engage in optically hazardous activities such as operating machinery or whichis; the patient storing of information of accordingly. Prescribes or other heads processorias should intern patients, that families, and their carginess bout the benefits and foliate accordingly. Prescribes or other heads processorias should intern patients, their families, and their carginess bout the benefits and foliate accordingly. Prescribes or health professional should estrate patients, their families, and their carginess for note the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The composition of the contents of the Medication Guide and to obtain assist them.

interpretables.

These agents —These agents (ammonium chloride, sodium acid phosphate, etc.) increase the concentration of the ionized as of the amphetamine molecule, thereby increasing urinary excretion. Both groups of agents lower blood levels and efficacy of

Unitary activities germs— rises separate interesting unriary excretion. Both groups of agents lover unous even emit consequences of the amphetamine molecule, thereby increasing unriary excretion. Both groups of agents lover unous even emit consequences accessed to the amphetamines and emitted by amphetamines. Advenops blockers—Advenops blockers—Advenops blockers—Advenops blockers—Advenops blockers—Advenops and possibly other tricyclic sause striking and sustained increases in the concentration of amphetamine with designamine or protriptyline and operated by the provision of amphetamines increasing their effect on the reades of norphisiphine and other monoarrines from advenops and protriptylines and other monoarrines from advenops of the protriptylines and other monoarrines. This sowing protriptylines are considered to the monoarrines from adventages of the protriptylines and other monoarrines. This sowing the protriptylines are considered to the monoarrines of the adventage of the protriptylines and other monoarrines. This sowing the protriptylines are considered to the monoarrines of the monoarrines of the monoarrines of the monoarrines and the trickles of amphetamines and can be used to treat amphetamines postering, and the protriptylines and the protriptylines and the protriptyline and the protriptyline and the protriptylines and the protriptylines and the monoarrines and the monoarrines and the monoarrines and the protriptyline and the monoarrines and the monoarri

Methenamine therapy — Urinary excretion of amphetamines is increased, and efficacy is reduced by acidifying agents used in metheramine therapy.

\*\*Managinaphine\*\*\* Amphetamines enhance the adrenergic effect of nonepirephrine.

\*\*Psendoarbital\*\*\* — Amphetamines may delay intestinal absorption of phenobarbital; co-administration of phenobarbital may produce a swensize autonomisera action.

synergistic antibonivulsant action.

Phenytoin — Amphetamines may delay intestinal absorption of phenytoin; co-administration of phenytoin may produce a synergistic

Prelayion—Antiphetanimes may obey meaning assorption or prelayon, co-administration of prelayon may produce a syveriginic anticionistical state classes of proposyphene overdosage, amphetamine CNS stimulation is potentiated and frail convolvisins can occur. Veraturu alkadods. Proposyphene—In cases of proposyphene—In cases of spiriturum alkadods. Drag takenotic proposyphene—In cases of spiriturum alkadods. Drag takenotic proposyphene control propos

Amothatamine (d to I enantinoner ratio of 3:1) did not adversely affect firtility or early embryonic development in the rat at doses of up to 20 m/gh/dys.

Pregnaner; Pregnancy: Catsgory C. Reproduction studies of Isidexamitation have not been performed.

Amphetamine (d to I enantinoner ratio of 3:1) had no apparent effects on embryotetal morphotogical development or survival when Amphetamine (d to I enantinoner ratio of 3:1) had no apparent effects on embryotetal morphotogical development or survival when the production of the

Usage in Nursing Mothers: Amphetamines are excited in human milk. Mothers taking amphetamines should be advised to retrain from mushing.

Provision: Any varies is indicated for use in hithiters and 6 to 12 years.

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Dass-related contrasses in food consumption, bodyweight gain, and crown-rump length were seen; after a four week drug-free recovery period bodyweight and crown-rump length were seen; after a four week drug-free recovery period bodyweight and crown-rump length were seen; after a four week drug-free recovery period bodyweight and crown-rump length were seen; after a four week drug-free recovery period bodyweight and crown-rump length were seen; after a four week drug-free recovery period bodyweight and crown-rump length were seen; after a four week drug-free recovery period bodyweight and crown-rump length were seen; after a four week drug-free recovery period bodyweight and crown-rump length were seen; after a four week drug-free recovery period bodyweight and crown-rump length were seen; after a four week drug-free recovery period bodyweight of the crown length of the seen seen and the seen of t

amphazimes in children have not been well established. Amphazimines are not recommended for use in children under 3 years of age. Gentaric Bies: Vyvanse has not been suitudied in the gentaric population.

ADVERSE EVENTS

The permarkelling development program for Vyvanse included exposures in a total of 404 participants in clinical trials (348 pediatric patients and 56 healthy adult subjects). Of these, 348 pediatric patients (ages 6 to 12) were evaluated in two controlled clinical studies (one parallel-group and one crossover), one open-faels extension study, and one single-desc clinical patramazology study. The information included in this section is based on data from the 4-week parallel-group controlled clinical trial in pediatric patients with ADH-0. Adverse events during procure were obtained primarily by general inquity and recorded by clinical investigators using terminology of adverse events, without Itsis grouping similar types of events during procure and adverse event of the type island. Health of the second proportion of includinglish who experienced, at less tonce, a treatment-emergent adverse event of the type island.

\*\*Reviewe event associated with discontinuation of treatment: Ten percent (21/218) of Vyvanse-treated patients discontinuation and considered to be drong-related (i.e., alexing to discontinuation of treatment: Ten percent (21/218) of Vyvanse-treated patients discontinuation and considered to be drong-related (i.e., alexing to discontinuation of treatment: Ten percent (21/218) of Vyvanse-treated patients discontinuation and considered to be drong-related (i.e., alexing to discontinuation of treatment; used to develop the development of the patients of the discontinuation and considered to be drong-related (i.e., alexing to discontinuation of the patients of the discontinuation and considered to be drong-related (i.e., alexing to discontinuation of th

Body System	Preferred Term	Vyvanse (n=218)	Placebo (n=72)
Gastrointestinal Disorders	Abdominal Pain Upper Dry Mouth Nausea Vomiting	12% 5% 6% 9%	6% 0% 3% 4%
General Disorder and Administration Site Conditions	Pyrexia	2%	1%
Investigations	Weight Decreased	9%	1%
Metabolism and Nutrition	Decreased Appetite	39%	4%
Nervous System Disorders	Dizziness Headache Somnolence	5% 12% 2%	0% 10% 1%
Psychiatric Disorders	Affect lability Initial Insomnia Insomnia Irritability Tic	3% 4% 19% 10% 2%	0% 0% 3% 0%

a rate twice that of the placebo group (Table 1) Upper vomiting, and decreased weight. The following additional adverse reactions the been associated with the use of amphetamine, amphetamine (d to I enanthomer ratio of 3:1), or Vyvanse: Cardiovascular: Palpitations, tachycardia, elevation of blood messule, sudden death, myocardial infarction. There have been fisclater reports of the placebook of the placebook of the placebook of maintainers. The properties of the placebook of central Nervous System: Psychotic episodes and commended doese, overstimusation, restless-ness, disziness, emphoria, dyskinesia, dysphona, depression, termor, headache, exercitation of motor and phonic its and Tourette's syndrome, saturus, strove.

motor and phonic its sand louretie's syndrome, sectures, Stroke. Baryness of the mouth, unpleasant laste, diarrhea, constipation. Allergic: Urticaria. hypersensitivity reactions including palopedema and analyhaxis. Serious skin rashes, Including Stevens Johnson Syndrome and toxic epidermal necrolysis have been reported. Endocrine: Impotence, changes in libido.

#### DRUG ABUSE AND DEPENDENCE

Controlled Substance Class
Vyvanse is classified as a Schedule II controlled substance.

Note: This table only includes those events for which the incidence in patients taking lyvanse is greater than the incidence in patients taking placebo.

Tolerance, other controlled specific patients that the incidence in patients taking placebo.

Tolerance, other corresponding objective dependence of the controlled specific patients who have increased the dospit and metal depress; or changes are also noted on the sleep EEG. Manifestations of chronic inforcation with amphitaments may include severe demantses, marked insortnis, irritability, hyperactivity, and personally changes. The most severe manifestation of chronic intoxication is systhosis, often chically indistinguishable from schizophretia.

invaluation is psychosis, often clinical indication included in the construction of changes. The most severe manifestation of chronic Human Studies in the construction of the constructio

Animal Studies in animal studies, lisdexamletamine produced behavioral effects qualitatively similar to those of the CNS stimulant d-amphetamine. In monkeys trained to self-administer occaine, intravenous lisdexamiletamine maintained self-administration at a rate that was statistically less than that for cocaine, but greater than that of placebo.

#### OVERDOSAGE

OVENDOSASE
Individual response to amphetamines varies widely. Toxic symptoms may occur idiosyncratically at low doses.
Symptoms: Manifestations of acute overdosage with amphetamines include restlessness, tremot, hyperrellexia, rapid respiration, contrasion, assaultiveness, hallucinations, panic states, hyperpress and inabdomylysis, Faligue and depression usually follow the central nervous system stimulation. Cardiovascular effects include artifythmias, hyperhesion or hypotension and circulatory collapse. Carsonitestical spatial poisoning is usually precised by Carsonitestical spatial poisoning is usually precised by

Considerabilities and symptoms include masses, virtually, warriers, and autonimate ranges, rating possible and controlled and

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#### **IMPORTANT SAFETY INFORMATION**

Vyvanse should not be taken by patients who have advanced arteriosclerosis; symptomatic cardiovascular disease; moderate to severe hypertension; hyperthyroidism; known hypersensitivity or idiosyncrasy to sympathomimetic amines; agitated states; glaucoma; a history of drug abuse; or during or within 14 days after treatment with monoamine oxidase inhibitors (MAOIs).

Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses in ADHD. Physicians should take a careful patient history, including family history, and physical exam, to assess the presence of cardiac disease. Patients who report symptoms of cardiac disease such as exertional chest pain and unexplained syncope should be promptly evaluated. Use with caution in patients whose underlying medical condition might be affected by increases in blood pressure or heart rate.

New psychosis, mania, aggression, growth suppression, and visual disturbances have been associated with the use of stimulants. Use with caution in patients with a history of psychosis, seizures or EEG abnormalities, bipolar disorder, or depression. Growth monitoring is advised during prolonged treatment.

Amphetamines have a high potential for abuse. Administration of amphetamines for prolonged periods of time may lead to drug dependence. Particular attention should be paid to the possibility of subjects obtaining amphetamines for non-therapeutic uses or distribution to others and the drugs should be prescribed or dispensed sparingly. Misuse of amphetamine may cause sudden death and serious cardiovascular adverse events.

The most common adverse events reported in clinical studies of Vyvanse were loss of appetite, insomnia, abdominal pain, and irritability.

Please see Brief Summary of Prescribing Information, including Boxed Warning, on adjacent page.

Reference: 1. Biederman J, Krishnan S, Zhang Y, et al. Efficacy and tolerability of lisdexamfetamine dimesylate (NRP-104) in children with attention-deficit/hyperactivity disorder: a phase III, multicenter, randomized, double-blind, forced-dose, parallel-group study. Clin Ther. 2007;29:450-463.

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The International Journal of Neuropsychiatric Medicine

#### **EDITOR'S LETTER**

# 730 Witches, Pumpkins, and Other Frightful Topics

Eric Hollander, MD, the Mount Sinai School of Medicine

#### **CASE REPORT**

# 764 Quetiapine for Mania Due to Traumatic Brain Injury

Timothy J. Oster, MD, HealthONE Spalding Rehabilitation Hospital; C. Alan Anderson, MD, University of Colorado School of Medicine; Christopher M. Filley, MD, University of Colorado School of Medicine; Hal S. Wortzel, MD, University of Colorado School of Medicine; and David B. Arciniegas, MD, HealthONE Spalding Rehabilitation Hospital

#### **ORIGINAL RESEARCH**

# 751 Romantic Attachment in Patients with Mood and Anxiety Disorders

Donatella Marazziti, MD; Bernardo Dell'Osso, MD; Mario Catena Dell'Osso, MD; Giorgio Consoli, MD; Alessandro Del Debbio, MD; Francesco Mungai, MD; Laura Vivarelli, MD; Francesco Albanese, MD; Armando Piccinni, MD; Paola Rucci, MD; and Liliana Dell'Osso, MD, University of Pisa

# 758 Aripiprazole in Juvenile Bipolar Disorder Comorbid with AttentionDeficit/Hyperactivity Disorder: An Open Clinical Trial

Silzá Tramontina, MD; Cristian Patrick Zeni, MD; Gabriel Ferreira Pheula, MD; Carla Ketzer de Souza, MD; and Luis Augusto Rohde, MD, Federal University of Rio Grande do Sul

# 771 Prevalence and Associated Factors for Suicidal Ideation` and Behaviors in Obsessive-Compulsive Disorder

Albina Rodrigues Torres, MD, PhD; Ana Teresa de Abreu Ramos-Cerqueira, PhD, Ricardo Cezar Torresan, MD; Mariana de Souza Domingues, MD; Ana Carolina R. Hercos; and Aron Barbosa C. Guimarães, Botucatu Medical School—Universidade Estadual Paulista "Julio de Mesquita Filho"— São Paulo State University

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# BECAUSE THE STAKES ARE HIGH Too many times I've seen how quickly the devastating effects of bipolar disorder can impact my patients' lives—and the damage that each episode can cause. Families torn apart. Careers ravaged. Relationships destroyed. The stakes are high. As a doctor, I fight every day to make sure that bipolar disorder will not win out. OL36807A 0206 ©2006, ELI LILLY AND COMPANY ALL RIGHTS RESERVED.