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Genetics in Eating Disorders:  
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Leptin Functioning in Eating Disorders  
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Exercise “Addiction” in Anorexia Nervosa:  
Model Development and Pilot Data  

Neuroimaging Studies in Eating Disorders  
The most common adverse events included loss of appetite, insomnia, abdominal pain, and emotional lability.

As with other psychostimulants indicated for ADHD, there is a potential for exacerbating motor and phonic tics and Tourette's syndrome. A side effect seen with the amphetamine class is psychosis. Caution also should be exercised in patients with a history of psychosis.
With efficacy that goes beyond adequate symptom control—to help them reach new heights

- Reduces symptoms to a level comparable to that of non-ADHD children
- Effectively addresses the core impairments of ADHD—inattention, hyperactivity, and impulsivity
- Once-daily dosing provides day-long improvement in academic productivity and social functioning

Abuse of amphetamines may lead to dependence. ADDERALL XR is contraindicated in patients with symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism and glaucoma, known hypersensitivity to this class of compounds, agitated states, history of drug abuse, or current or recent use of MAO inhibitors. ADDERALL XR should be prescribed with close physician supervision.
**INDICATIONS**

ADDERALL XR* is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). The efficacy of ADDERALL XR in the treatment of ADHD was established on the basis of two controlled, 8-week placebo-controlled clinical trials conducted in children ages 6 to 12 years. The treatment effects obtained with ADDERALL XR in these studies were consistent with the positive results previously obtained withoral ADDERALL* (a racemic mixture of d- and l-amphetamine salts). Consequently, the treatment effects obtained with ADDERALL XR in these studies were consistent with the positive results previously obtained with oral ADDERALL* (a racemic mixture of d- and l-amphetamine salts).

**PRECAUTIONS**

- The maximum recommended daily dose of ADDERALL XR is 30 mg/day in children 6 to 12 years of age, 20 mg/day in adolescents 13 to 17 years of age, and 15 mg/day in adults. The dose should be titrated gradually and carefully, and the patient should be monitored closely for response and adverse effects.

- The use of ADDERALL XR is generally not recommended in patients with a history of drug abuse. During or within 14 days following the administration of ADDERALL XR, the patient should be observed for any evidence of drug abuse.

- ADDERALL XR should be prescribed or dispensed at one time in order to minimize the potential for drug dependence and overdose. The patient should be instructed to take the medication exactly as directed by the prescriber.

- ADDERALL XR has not been studied in the geriatric population. The use of ADDERALL XR in the elderly population has not been systematically investigated. The safety and efficacy of ADDERALL XR in the elderly population have not been established. In the elderly, the potential for increased sensitivity to the effects of amphetamines should be considered.

- ADDERALL XR has not been studied in patients with a history of drug abuse. During or within 14 days following the administration of ADDERALL XR, the patient should be observed for any evidence of drug abuse.

**ADVERSE EVENTS**

- The premarketing development program for ADDERALL XR included exposures in a total of 685 participants in clinical trials (615 patients, 70 healthy adult subjects). These participants received ADDERALL XR at daily doses up to 30 mg. The 615 patients (ages 6 to 12) were evaluated in two controlled clinical studies, one open-label clinical study, and one single-dose clinical pharmacology study (N=20). Safety data on all patients are included in the discussion that follows. Adverse reactions were assessed by collecting adverse events, results of physical examinations, vital signs, and laboratory analyses. Children 6 to 17 years of age were included in the controlled clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, provide some relative indication of overall frequencies of reported events and are useful in the comparison of the relative safety of one drug candidate with that of other drugs of a similar class. The overall frequency of adverse events reported in clinical trials is likely to be overestimated as a result of the inherent tendency to report adverse events and because some adverse reactions are considered by the investigator to be related to the drug treatment. The cited frequencies also reflect the investigators’ awareness of the possibility of drug-related adverse reactions and, in many cases, the use of a more stringent definition of adverse reactions for events that are considered related to the drug treatment. The cited frequencies also reflect the investigators’ awareness of the possibility of drug-related adverse reactions and, in many cases, the use of a more stringent definition of adverse reactions for events that are considered related to the drug treatment.

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<th>Body System</th>
<th>Preferred Term</th>
<th>% Placebo</th>
<th>% ADDERALL XR</th>
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<tr>
<td>General</td>
<td>Amphetamine Abuse (psychostimulant)</td>
<td>14%</td>
<td>11%</td>
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<td>Accidental Injury</td>
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<td>Dizziness</td>
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<td>Infection</td>
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<td>Weight loss</td>
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<td></td>
<td>Emotional Lability</td>
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<td>Metabolism/Nutrition</td>
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<td>Weight loss</td>
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**ADVERSE EVENTS ASSOCIATED WITH DISCONTINUATION OF TREATMENT**

- Adverse events associated with discontinuation of treatment in a placebo-controlled study of up to 6 weeks during 24% (4/102) of ADDERALL XR treated patients discontinued due to adverse events (including 3 patients with loss of appetite, one of whom also reported insomnia) compared to 3.7% (5/189) receiving placebo. The most common adverse events associated with discontinuation of ADDERALL XR in controlled and uncontrolled, multiple-dose clinical trials (N=486) are presented below: Over half of these patients were exposed to ADDERALL XR for 12 months or more. Adverse event % of patients discontinuing (N=486)

- **Aphasia (loss of speech)**: 2.9%
- **Anorexia**: 1.5%
- **Weight loss**: 6.0%
- **Emotional lability**: 1.0%
- **Irritability**: 1.0%

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Introduction

CNS Spectrums is an Index Medicus journal that publishes original scientific literature and reviews on a wide variety of neuroscientific topics of interest to the clinician on a monthly basis. Our mission is to provide physicians with an editorial package that will enhance and increase their understanding of neuropsychiatry; therefore, manuscripts that address crossover issues between neurology and psychiatry will be given immediate priority.

Scope of Manuscripts

CNS Spectrums will consider and encourage the following types of articles for publication:

Original Research presents methodologically sound original data.

Reviews are comprehensive articles summarizing and synthesizing the literature on various neuropsychiatric topics and presented in a scholarly and clinically relevant fashion. Diagnostic and treatment algorithms should be designed to aid the clinician in diagnosis and treatment. Letters to the Editor will be considered and are encouraged for publication. Letters to the Editor will be considered and are encouraged for publication. All letters will be edited for style, clarity, and length.

Manuscript Submission

General Information Two copies of the manuscript with a letter on the author's letterhead should be submitted to Jack M. Gorman, MD, Editor (or, in Europe, to Joseph Zohar, MD, International Editor), c/o MBL Communications, 333 Hudson Street, 7th Floor, New York, NY 10013. Authors are also required to submit their manuscripts on computer disk in Microsoft Word format. Disks should be labeled with the word processing program, title of paper, and lead author's name. Accepted manuscripts will be edited for clarity and style.

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Peer Review Authors must provide three to five names of qualified potential reviewers with no conflict of interest in reviewing the work. Contact information with affiliations and e-mail address should be included. Peer review is anonymous.

Manuscript Preparation

Length Reviews and Original Research should not exceed 5,000 words (excluding References). Diagnostic and treatment algorithms should contain an introduction, flowcharts or a series of graphs, and a concise summary. Letters should not exceed 1,500 words. Single Case Reports should not exceed 3,750 words and may be submitted with a photograph, if applicable.

Please note: If your article is Original Research, it should be formatted as: Abstract (100-200 words); Introduction, Methods; Findings; Discussion; Conclusion; References (numbered and comprehensive list).

Spacing and Pagination One space should be left after commas and periods. Manuscripts should be double-spaced and numbered.

Abstract Authors must provide a brief abstract of 100-200 words.

Focus Points Please provide three to six points that dictate the main focus of the manuscript and clearly illustrate what you are trying to convey in the article.

Figures/Tables Please provide original figures and/or tables if content is amenable to it.

References Please use American Medical Association style. References should be superscripted in text, then numbered, and comprehensive in list. See the following examples:


Continuing Medical Education Authors must submit six multiple-choice questions (three Type A and three Type K), with answers.

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Authors must include a statement about all forms of support, including grant and pharmaceutical support, affiliations, and honoraria received for past and present material. Such information may, at the editor's discretion, be shared with reviewers. If the article is accepted for publication, the editors will consult with the authors as to whether this information should be included in the published paper.

Submission Checklist

☐ Original manuscript plus one copy, with cover letter on author's letterhead
☐ Copies of permission letters to reproduce previously published and unpublished material
☐ A brief abstract of the article
☐ Six CME multiple-choice questions with answers
☐ Three to six focus points
☐ Disk labeled with the word processing program, title of paper, and lead author's name
☐ Names and affiliations of three to five potential peer reviewers
ed TSH lev*, 3 had similar simultaneous low T4 levels. Cholesterol and triglycerides elevations: In schizophrenia, this relationship to use of SEROQUEL has not been established, other drugs with alpha-adrenergic blocking effects have been. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events reported occurred during treatment with SEROQUEL; they were not necessarily caused by it. Events are (ur-}
NOW FDA approved for MANIA IN BIPOLAR DISORDER

Well Accepted!

Another great reason to prescribe

- Effective so patients improve
- Trusted tolerability so patients can stay on treatment

The safety and efficacy of SEROQUEL in pediatric patients have not been established. Patients should be periodically reassessed to determine the need for continued treatment. Prescribing should be consistent with the need to minimize the risk of tardive dyskinesia, seizures, and orthostatic hypotension. A rare condition referred to as neuroleptic malignant syndrome (NMS) has been reported with this class of medications, including SEROQUEL.

There have been reports of diabetes mellitus and hyperglycemia-related adverse events associated with the use of atypical antipsychotics, including SEROQUEL.

The most common adverse events associated with the use of SEROQUEL were somnolence, dry mouth, dizziness, constipation, asthenia, abdominal pain, postural hypotension, pharyngitis, SGPT increase, dyspepsia, and weight gain.

In bipolar mania trials, withdrawal rates due to adverse events were similar to placebo for SEROQUEL as monotherapy (SEROQUEL 5.7%, placebo 5.1%) and adjunct therapy (SEROQUEL plus lithium or divalproex 3.6%, lithium or divalproex alone 5.9%).


To prevent medication errors, write “SEROQUEL” clearly on your Rx pad. Spell “SEROQUEL” clearly over the phone. Please see Brief Summary of Prescribing Information on following page.

First-line treatment

www.SEROQUEL.com
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Assessing Current Practice in Alzheimer’s Disease

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**CNS SPECTRUMS ONLINE**

This month’s issue of CNS Spectrums, as well as a host of educational resources, enduring materials, and archived issues, is available at www.cnsspectrums.com.
ZONEGRAN is indicated as adjunctive therapy in the treatment of partial seizures in adults with epilepsy. In clinical trials, the most common adverse events that occurred with ZONEGRAN were somnolence, dizziness, anorexia, headache, nausea, and agitation/irritability.

*Can also be dosed twice daily.

Please see brief summary of Prescribing Information on adjacent page.

CONTRIBUTIONS
ZONEGRAN is contraindicated in patients who have demonstrated hypersensitivity to sulfaamides or zonisamide.

WARNINGs
Potentially Fatal Reactions to Sulfonamides: Fatalities have occurred following the ingestion of sulfonamides (sulfamethizide is a sulfonamide) including Stevens-Johnson syndrome, toxic epidermal necrolysis, leukopenia, neutropenia, agranulocytosis, erythroblastopenia, aplastic anemia, and toxic epidermal necrolysis.

Sulfa drugs are contraindicated during pregnancy (see Pregnancy: Pregnancy Category C). Fetal abnormalities or discontinuation of zonisamide immediately. Specific experience with sulfonamide use in pregnancy is limited. There have been no reports of human or animal studies regarding the effects of zonisamide on fertility (see Fertility: Controlled Human Reproduction).

The mechanism for the teratogenic effect in the rat is not known. Studies in both rats and dogs have demonstrated that defects were prominent in both rats and dogs.

Following administration of zonisamide (10, 30, or 60 mg/kg/day) to pregnant dogs during organogenesis, increased numbers of maternal deaths occurred, including serum CPK and aldolase levels. If elevated, in the absence of other cause such as trauma, granulocytopenia, etc., tapering or/or discontinuation of zonisamide should be considered and appropriate therapy initiated. Serum CPK levels and signs and symptoms of pancreatitis should have pancreatic, lipase and amylase levels monitored. If pancreatitis is evident, the drug may be discontinued.

Information for Patients
Patients should be advised as follows:
1. ZONEGRAN may produce drowsiness, especially at higher doses or early in treatment, and the patient should avoid operating other complex machinery until they have gained experience. It is not sufficient to determine whether it affects their performance.
2. Patients should contact their physician immediately if a skin rash develops or seizures worsen.
3. Patients should continue zonisamide immediately if they develop signs or symptoms, such as sudden back pain, abdominal pain, or blood in the urine, that could indicate a dose-related increase in urate, which could lead to gout or reduce the risk of stone formation, particularly in those with a positive family history.
4. Patients should contact their physician immediately if a child has been taking ZONEGRAN and is not sweating as usual.

Because zonisamide can cause hemolytic complications, patients should contact their physician immediately if they develop clinical jaundice, abdominal pain, and/or blood in the urine, that could indicate acute hepatic necrosis, agranulocytosis, aplastic anemia, and other drug-related events.

Drugs that induce liver enzymes can increase the metabolism and clearance of zonisamide. Zonisamide should not be used in patients with epilepsy who are taking enzyme-inducing AEDs such as phenytoin, carbamazepine, or valproate during clinical trials. Zonisamide did not inhibit mixed function oxidase enzymes (cytochrome P450) as measured in human liver microsomal fractions. This is in contrast to the in vitro results (see PRECAUTIONS, Effect on Renal Function Subsection).

Drugs that induce liver enzymes can increase the metabolism and clearance of zonisamide. Zonisamide should not be used in patients with epilepsy who are taking enzyme-inducing AEDs such as phenytoin, carbamazepine, or valproate during clinical trials. Zonisamide did not inhibit mixed function oxidase enzymes (cytochrome P450) as measured in human liver microsomal fractions. This is in contrast to the in vitro results (see PRECAUTIONS, Effect on Renal Function Subsection).

Seizures and Withdrawal: As with other AEDs, abrupt withdrawal of zonisamide can produce seizures. A gradual withdrawal is recommended. The incidence of seizures is difficult to estimate, especially in studies that do not use a standard definition. It is not clear whether the incidence of seizures is increased in patients treated with zonisamide compared to those treated with placebo. Although from studies of open-label treatment, the rate of seizures with zonisamide is not increased compared to placebo.

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The low effect dose for malformations produced peak maternal plasma zonisamide levels (25 ug/mL) about 0.5 times the highest human levels. In cynomolgus monkeys, administration of zonisamide (10 or 20 mg/kg/day) to pregnant animals during organogenesis resulted in embryo-fetal deaths at both doses. The possibility that these deaths were due to malformations cannot be ruled out. The lowest embryo-fetal death dose in monkeys was associated with peak maternal plasma zonisamide levels (5 ug/mL) approximately 0.1 times the highest levels measured in patients at the MRHD.

In a mouse embryo-fetal development study, treatment of pregnant mice with zonisamide (50, 100, or 200 mg/kg/day) during the period of organogenesis resulted in increased incidences of fetal malformations (skeletal) and/or craniofacial defects in all dose tested. The low dose was approximately 1.5 times the MRHD on a mg/m² basis. In rats, incidences of all malformed fetuses (cardiovascular defects and variations [persistent ductus of thyrocoid, decreased ossification]) were observed among the offspring of dams treated with zonisamide (20, 60, or 200 mg/kg/day) throughout organogenesis at all doses. The low effect dose is approximately 0.2 times the MRHD on a mg/m² basis.

Perinatal death was increased among the offspring of rats treated with zonisamide (50, 100, or 600 mg/kg/day) from 10 days of gestation to term. The highest dose was approximately 1.1 times the MRHD on a mg/m² basis. In addition, there has been an increased perinatal mortality rate among the offspring of rats treated with zonisamide (125, 250, or 500 mg/kg/day) from gestation day 16 through organogenesis at all doses. The low effect dose is approximately 0.1 times the MRHD on a mg/m² basis. Rarely, perinatal deaths have been observed among the offspring of rats treated with zonisamide (50, 100, or 200 mg/kg/day) from 10 days of gestation to term. The highest dose was approximately 1.1 times the MRHD on a mg/m² basis. In rats, cardiovascular malformations were found in newborn animals with zonisamide (125, 250, or 500 mg/kg/day). The low effect dose for malformations produced peak maternal plasma zonisamide levels (25 ug/mL) approximately 0.1 times the highest levels measured in patients at the MRHD.

Perinatal death was increased among the offspring of rats treated with zonisamide (50, 100, or 600 mg/kg/day) from 10 days of gestation to term. The highest dose was approximately 1.1 times the MRHD on a mg/m² basis. In addition, there has been an increased perinatal mortality rate among the offspring of rats treated with zonisamide (125, 250, or 500 mg/kg/day) from gestation day 16 through organogenesis at all doses. The low effect dose is approximately 0.1 times the MRHD on a mg/m² basis. Rarely, perinatal deaths have been observed among the offspring of rats treated with zonisamide (50, 100, or 200 mg/kg/day) from 10 days of gestation to term. The highest dose was approximately 1.1 times the MRHD on a mg/m² basis. In rats, cardiovascular malformations were found in newborn animals with zonisamide (125, 250, or 500 mg/kg/day). The low effect dose for malformations produced peak maternal plasma zonisamide levels (25 ug/mL) approximately 0.1 times the highest levels measured in patients at the MRHD.

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Perinatal death was increased among the offspring of rats treated with zonisamide (50, 100, or 600 mg/kg/day) from 10 days of gestation to term. The highest dose was approximately 1.1 times the MRHD on a mg/m² basis. In addition, there has been an increased perinatal mortality rate among the offspring of rats treated with zonisamide (125, 250, or 500 mg/kg/day) from gestation day 16 through organogenesis at all doses. The low effect dose is approximately 0.1 times the MRHD on a mg/m² basis. Rarely, perinatal deaths have been observed among the offspring of rats treated with zonisamide (50, 100, or 200 mg/kg/day) from 10 days of gestation to term. The highest dose was approximately 1.1 times the MRHD on a mg/m² basis. In rats, cardiovascular malformations were found in newborn animals with zonisamide (125, 250, or 500 mg/kg/day). The low effect dose for malformations produced peak maternal plasma zonisamide levels (25 ug/mL) approximately 0.1 times the highest levels measured in patients at the MRHD.