ORIGINAL RESEARCH

D-cycloserine Inhibits Amygdala Responses During Repeated Presentations of Faces
J.C. Britton, A.L. Gold, E.J. Feczko, S.L. Rauch, D. Williams, and C.I. Wright

REVIEW ARTICLES

The Effect of Pathological Gambling on Families, Marriages, and Children
M.C. Shaw, K.T. Forbush, E. Rosenman, and D.W. Black

Beyond Intravenous Thrombolysis
K. Lee, S. Muppidi, F. Siddiq, C. Pineda, D.G. Brock, and R.D. Bell

Selective Unilateral Autonomic Activation: Implications for Psychiatry
D.S. Shannahoff-Khalsa

CASE REPORT

Serotonin Syndrome in Elderly Patients Treated for Psychotic Depression with Atypical Antipsychotics and Antidepressants: Two Case Reports
I. Kohen, M.L. Gordon, and P. Manu

TRENDS IN PSYCHOPHARMACOLOGY

The Genetics of Schizophrenia Converge Upon the NMDA Glutamate Receptor
S.M. Stahl

COMMUNIQUE

Ziprasidone-Associated Mania in a Case of Obsessive-Compulsive Disorder
**Vyvanse** (lisdexamfetamine dimesylate)

**Glu Dose**

**Brief Summary**
Consult the Fact Sheet for prescriber and patient information.

**ADVERSE REACTIONS**

**Sudden death and Serious Cardiovascular Adverse Events**

Sudden deaths, mostly in young men, have been associated with the use of stimulants for ADHD. Although the risk is small, parental and caregiver education and monitoring are important aspects of management for all patients treated with stimulants. 

**Cardiovascular**

- **Palpitations**
- **Tachycardia**
- **Elevation in blood pressure**
- **Elevations in heart rate**
- **Sudden deaths**
- **Myocardial infarction**
- **Stroke**

**Respiratory**

- **Apnea**

**Central Nervous System**

- **Psychotic episodes**
- **Depression**
- **Tremor**
- **Headache**
- **Exacerbation of Tourette's syndrome**
- **Exacerbation of tic disorder**

**Skin**

- **Urticaria**
- **Hypersensitivity reactions**
- **Severe skin rash**
- **Stevens-Johnson syndrome**
- **Allergic**

**Gastrointestinal**

- **Diarrhea**
- **Constipation**

**Cardiac**

- **Cardiomyopathy**
- **Arrhythmias**
- **Other serious cardiac problems**

**Special Systems**

- **Visual disturbances**
- **Dizziness**
- **Somnolence**

**Weight**

- **Temporary slowing in growth rate**

**Other**

- **Increased appetite**
- **Psychiatric**
- **Digestive**
- **Endocrine**
- **Renal**
- **Reproductive**

**What is the mean change in blood pressure?**

The mean changes in blood pressure (systolic/diastolic) are approximately 4/3 mm Hg in adults under 18 years of age. In children aged 7 to 12 years, the mean changes in blood pressure (systolic/diastolic) are approximately 3/1 mm Hg. The mean change in heart rate is approximately 3 bpm in adults under 18 years of age. In children aged 7 to 12 years, the mean change in heart rate is approximately 6 bpm.

**What is the mean change in weight?**

The mean change in weight is approximately 2 cm less growth in height and 2.7 kg less growth in weight in adults under 18 years of age. In children aged 7 to 12 years, the mean change in weight is approximately 2 cm less growth in height and 2.7 kg less growth in weight.

**What is the mean change in growth rate?**

The mean change in growth rate is approximately 2.6 cm less growth in height and 2.7 kg less growth in weight in adults under 18 years of age. In children aged 7 to 12 years, the mean change in growth rate is approximately 2.6 cm less growth in height and 2.7 kg less growth in weight.

**What is the mean change in body mass index (BMI)?**

The mean change in body mass index (BMI) is approximately 0.4 kg/m² in adults under 18 years of age. In children aged 7 to 12 years, the mean change in body mass index (BMI) is approximately 0.4 kg/m².

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INTRODUCING

Vyvanse (lisdexamfetamine dimesylate) capsules

The First Prodrug Stimulant

Significant efficacy throughout the day, even at 6 PM

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; agitation; 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.


This information is brought to you by

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A Taste of the Programme:

**Chairperson:** Dan J. Stein, MD, PhD

- **Anxiety Disorders in Schizophrenia**
  David Castle, MD
  *University of Melbourne (Australia)*

- **Endophenotypes in Obsessive-Compulsive Disorder**
  Naomi Fineberg, MD
  *University of Hertfordshire (United Kingdom)*

- **Substance Abuse and Anxiety Disorders**
  Marc Schuckit, MD
  *University of California at San Diego (United States)*

- **Optimising Diagnosis in the Community**
  Christer Allgulander, MD
  *Karolinska Institute (Sweden)*

- **Repetitive Transcranial Magnetic Stimulation in Anxiety Disorders**
  Jack van Honk, PhD
  *Utrecht University (Netherlands)*

*And a range of other expert speakers*

**Dates to Remember:**

- **November 9, 2007** — Closing date for electronic abstracts
- **January 11, 2008** — Closing date for early registration
- **February 22, 2008** — Closing date for symposium registration

For more information and to register for the conference, please visit: www.mentalhealthsa.co.za/anxietyconference/registration.php

or contact: Arlene Kleinhans at arlene@sun.ac.za

*Please note this conference takes place immediately after the International Society for Affective Disorders meeting taking place March 14–17 at the Arabella Sheraton Hotel*
EDITOR'S LETTER

577 August and the Central Nervous System
Eric Hollander, MD, the Mount Sinai School of Medicine

CASE REPORT

596 Serotonin Syndrome in Elderly Patients Treated for Psychotic Depression with Atypical Antipsychotics and Antidepressants: Two Case Reports
Izchak Kohen, MD, Zucker Hillside Hospital; Marc L. Gordon, MD, Zucker Hillside Hospital; and Peter Manu, MD, Zucker Hillside Hospital

ORIGINAL RESEARCH

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REVIEW ARTICLES

609 Beyond Intravenous Thrombolysis
Kiwon Lee, MD, Columbia University College of Physicians and Surgeons; Srikanth Muppidi, MD, Thomas Jefferson University; Farhan Siddiq, MD, Thomas Jefferson University; Carissa Pineda, MD, Thomas Jefferson University; David G. Brock, MD, Thomas Jefferson University; and Rodney D. Bell, MD, Thomas Jefferson University

615 The Effect of Pathological Gambling on Families, Marriages, and Children
Martha C. Shaw, BA, University of Iowa Roy J. and Lucille A. Carver College of Medicine; Kelsie T. Forbush, MA, University of Iowa Roy J. and Lucille A. Carver College of Medicine; Jessica Schinder, BA, University of Iowa Roy J. and Lucille A. Carver College of Medicine; Eugene Rosenman, MD, Private Practice; and Donald W. Black, MD, University of Iowa Roy J. and Lucille A. Carver College of Medicine

625 Selective Unilateral Autonomic Activation: Implications for Psychiatry
David S. Shannahoff-Khalsa, BA, University of California-San Diego

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Anxiety, insomnia, low energy
Currently on an SSRI*
Still suffering

It may be time to make a change

Still depressed?

Break the Cycle with EFFEXOR XR

* Patients currently on an SSRI should be evaluated following an adequate trial.

IMPORTANT TREATMENT CONSIDERATIONS

Suicidality and Antidepressant Drugs
Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. EFFEXOR XR is not approved for use in pediatric patients.

• EFFEXOR XR is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs).

• Adult and pediatric patients taking antidepressants can experience worsening of their depression and/or the emergence of suicidality. All patients should be monitored appropriately and observed closely for clinical worsening and suicidality, especially at the beginning of drug therapy, or at the time of increases or decreases in dose. Anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, and mania have been reported and may represent precursors to emerging suicidality. Stopping or modifying therapy should be considered especially when symptoms are severe, abrupt in onset, or not part of presenting symptoms.

• EFFEXOR XR with EFFEXOR XR is coadministered with other drugs that may affect the serotonergic neurotransmitter systems. Concomitant use of EFFEXOR XR with MAOIs is contraindicated. If concomitant use of EFFEXOR XR with an SSRI, SNRI, or a triptan is clinically warranted, careful observation of the patient is advised. Concomitant use of EFFEXOR XR with tryptophan supplements is not recommended.

• Treatment with venlafaxine is associated with sustained increases in blood pressure (BP) in some patients. Postmarketing cases of elevated BP requiring immediate treatment have been reported. Pre-existing hypertension should be controlled. Regular BP monitoring is recommended.

• Mydriasis has been reported in association with venlafaxine; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored.

• Abrupt discontinuation or dose reduction has been associated with discontinuation symptoms. Patients should be counseled on possible discontinuation symptoms and monitored while discontinuing the drug; the dose should be tapered gradually.

Please see brief summary of Prescribing Information on adjacent pages.

ONCE-DAILY
VENLAFAXINE HCI
EFFEXOR XR® EXTENDED
RELEASE CAPSULES

The change they deserve.
Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicide thoughts or behavior in children, adolescents, and young adults in short-term studies of depression and other psychiatric disorders at a relative risk of about 2.1 (range, 1.1-3.8) during the first 4 months of treatment. Any increased risk of suicidality with antidepressants is greatest within the first 1-2 months of treatment. Risks and benefits of use in other age groups should be considered. Treatments shown to be effective in adults are not necessarily effective in children or adolescents.

Special Considerations

Weight loss

Weight loss was seen in patients aged 6-17 receiving Effexor XR. More Effexor XR patients than placebo patients aged 6-17 had >7% weight loss (11% vs. 6%). Weight loss was seen in only 0.3% of placebo patients. In the 6-month MDD study, children and adolescents had height increases less than expected based on data from age- and sex-matched non-depressed controls. The differences were statistically significant for females (n=220): mean increase of 0.3 cm (95% CI: 0.1, 0.5) for Effexor XR patients vs. -0.2 cm (95% CI: -0.5, 0.1) for placebo patients (P=0.041). This difference was not statistically significant for males (n=225): mean increase of 0.9 cm (95% CI: -0.2, 2.0) for Effexor XR patients vs. 0.7 cm (95% CI: -0.3, 1.8) for placebo patients (P=0.13).

In short-term MDD trials, 7% of Effexor XR patients had >5% weight loss and 0.1% discontinued for weight loss. In 12-week PD trials, 3% of Effexor XR patients had >7% loss of body weight, and 3% of placebo patients had weight loss of at least 3.5% in both MDD and GAD studies. (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 2,550 patients, 10 of which included placebo-controlled trials of venlafaxine. In total, 1,211 patients were randomized to placebo and 1,341 patients were randomized to venlafaxine. In 2 of these placebo-controlled studies, patients were randomized to placebo and venlafaxine in 6 trials (12-week MDD studies), 8 trials (12-week PD studies), and 4 trials (6-month PD studies). In both studies, venlafaxine \( \left( 11.5 \right) + 3.0 \) mg/kg/day compared to placebo (P<0.001) or placebo patients (P<0.001).


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Recurrent MDD

The effect on labor and delivery in humans is unknown. The available information on venlafaxine and ODV use during pregnancy is more limited than that for other antidepressants. However, venlafaxine-induced reduction of the PRL level has been reported to result in galactorrhea and lactation in some patients who were not previously lactating. The known effects of ODV on the PRL level are indistinguishable from those of venlafaxine. Given the known effects of venlafaxine, the potential risks of venlafaxine and ODV use during pregnancy should be considered in light of the potential benefits. There are no adequate and well-controlled studies in pregnant women, except for studies assessing the effects of venlafaxine on labor and delivery. Therefore, venlafaxine and ODV should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Serum Levelsparison

The mean serum levels of venlafaxine and ODV were not altered in a single dose of diazepam did not appear to affect the PK of either venlafaxine or ODV. Venlafaxine did not have any effect on the PK of the PK-1,200 mg L-dopa, 200 mg ergotamine tartrate, or 10 mg propranolol, or any of the psychotropic effects induced by diazepam. Sedation and drowsiness related to venlafaxine and ODV were not dose-related. The single dose of diazepam had no effect on the PK of venlafaxine. Diazepam-induced changes in blood pressure were not compared to those observed in placebo patients treated for at least 3 months in trials. Consider measurement of serum cholesterol levels during long-term treatment. 3% of Effexor XR patients had treatment-emergent hypothyroidism. There have been a few cases of thyroid cancer in a small number of patients treated with antidepressants. All patients should be screened to determine if they are at risk for bipolar disorder; such screening should include a detailed history, physical examination, and laboratory studies. If there are risks that might be significant, consideration should be given to choosing an alternative treatment or monitoring patients more frequently than once every 1-4 weeks. The potential presence of these events in venlafaxine patients who present with progressive dyspnea, cough, or chest pain should be immediately investigated. At least 7 days should be allowed after stopping venlafaxine before starting an MAOI. Pre-existing hypertension should be controlled. Regular monitoring of BP is recommended. For patients experiencing sustained increase in BP, consider either dose reduction or treatment withdrawal.

Complications can arise immediately upon delivery. Reports include respiratory distress, cyanosis, apnea, seizures, and decreased or absent reflexes. Seizures, in preterm and/or low-birth weight infants, have occurred with both venlafaxine and ODV use during pregnancy. In some cases, it is consistent with serotonin syndrome. When treating a pregnant woman with Effexor XR, use with caution in such patients. Patients should be advised of the risk for neonatal abstinence syndrome. In some cases, it is consistent with serotonin syndrome. When treating a pregnant woman with Effexor XR, use with caution in such patients. Patients should be advised of the risk for neonatal abstinence syndrome. In cases of neonatal abstinence syndrome, the treatment of choice is supportive care, including assisted ventilation, drug therapy, and medical monitoring. The use of maternal venlafaxine or ODV may also be associated with impaired psychomotor and psychometric effects induced by ethanol. Consideration should be given to choosing an alternative treatment or monitoring patients more frequently than once every 1-4 weeks. The potential presence of these events in venlafaxine patients who present with progressive dyspnea, cough, or chest pain should be immediately investigated. At least 7 days should be allowed after stopping venlafaxine before starting an MAOI. Pre-existing hypertension should be controlled. Regular monitoring of BP is recommended. For patients experiencing sustained increase in BP, consider either dose reduction or treatment withdrawal.

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effective in the pediatric population have not been established (see BOX WARNING and WARNINGS: Clinical Worsening and Suicide Risk). No studies have adequately assessed the impact of Effexor XR on growth, development and maturation of children and adolescents. Studies suggest Effexor XR may adversely affect weight and height (see PRECAUTIONS—General, Changes in Height and Changes in Weight). Should the decision be made to treat a pediatric patient with Effexor XR, regular monitoring of weight and height is recommended during treatment, particularly in long-term use. The safety of Effexor XR for pediatric patients has not been assessed for chronic treatment of 6 months or longer in patients aged 11-17. Adverse events and drug interactions considered to be clinically relevant were similar to those observed in adult patients. The precautions for adults apply to pediatric patients.

Geriatric Use—Older patients may be more susceptible to side effects such as falls, syncope, and postural hypotension. Therefore, caution should be exercised in the use of Effexor XR in the elderly, as adverse events and drug interactions may be more severe in this population compared to younger patients. Elderly patients have a higher pre-existing burden of suicide risk factors than SSRI-treated patients. The extent to which the finding of age-related increases in the proportion of patients meeting criteria for mania or hypomania compared to the population as a whole—Frequent: chest pain substernal, chills, fever, neck pain; Infrequent: face edema, intentional injury, malaise, moniliasis, neck rigidity, pelvic pain, photosensitivity reaction, suicide attempt, withdrawal syndrome; Rare: chest pain, back pain, musculoskeletal pain, chest discomfort, septicemia, shock-like symptom complex, systemic symptoms and signs of anaphylactic, urticarial, angioedema, respiratory distress, hypotension, hypoxia, dyspnea, and cardiac arrest. Treatment should consist of those general measures appropriate to the patient's condition. Ambulatory electrocardiogram and echocardiography have been performed in the study population.

ADVERSE REACTIONS: The most common adverse events observed in patients treated with MDD, 200-1600 mg/day, and with 200 mg/day in patients with depression were nausea, headache, dizziness, anxiety, insomnia, nervousness, and crying. ADVERSE REACTIONS: The most common adverse events reported in patients treated with Effexor XR short-term placebo-controlled MDD, generalized anxiety disorder (GAD), social anxiety disorder (SAD), and/or panic disorder (PD) trials (incidence ≥10% and ≥2x that of placebo) were anorexia, asthenia, constipation, dizziness, nausea, nervousness, somnolence, and sweating.

Effexor XR provides supplies feedback and updates about these patient calls to you, their physician.

Diologue offers patient access to a call center to speak with a health care provider to reinforce your efforts.

Encourage your EFFEXOR XR patients to enroll in Dialogues by calling 866-313-3737—and you will be invited to mddpatientsupport.com.

• The most common adverse events reported in EFFEXOR XR short-term placebo-controlled MDD, generalized anxiety disorder (GAD), social anxiety disorder (SAD), and/or panic disorder (PD) trials (incidence ≥10% and ≥2x that of placebo) were anorexia, asthenia, constipation, dizziness, nausea, nervousness, somnolence, and sweating.

The change they see is a unique patient support and education program that is designed to help you foster successful therapy.

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The change they see is a unique patient support and education program that is designed to help you foster successful therapy.

Dialogues offers patient access to a call center to speak with a health care provider to reinforce your efforts.
You can prescribe Rozerem for as long as you need to*

Clinical studies show no evidence of potential abuse, dependence, or withdrawal.

- **First and only**—nonscheduled prescription insomnia medication...not a controlled substance and can be prescribed for long-term use.

- **First and only**—prescription insomnia medication that targets the normal sleep-wake cycle

- **First and only**—prescription insomnia medication with no evidence of abuse potential in clinical studies

- **First and only**—prescription insomnia medication that does not promote sleep by CNS depression

- **One simple 8-mg dose**

*Rozzerem® (ramelteon) is indicated for the treatment of insomnia characterized by difficulty with sleep onset. Rozzerem can be prescribed for long-term use.

**Important safety information**

Rozzerem should not be used in patients with hypersensitivity to any components of the formulation, severe hepatic impairment, or in combination with fluvoxamine. Failure of insomnia to remit after a reasonable period of time should be medically evaluated, as this may be the result of an unrecognized underlying medical disorder. Hypnotics should be administered with caution to patients exhibiting signs and symptoms of depression. Rozzerem has not been studied in patients with severe sleep apnea, severe COPD, or in children or adolescents. The effects in these populations are unknown. Avoid taking Rozzerem with alcohol. Rozzerem has been associated with decreased testosterone levels and increased prolactin levels. Health professionals should be mindful of any unexplained symptoms possibly associated with such changes in these hormone levels. Rozzerem should not be taken with or immediately after a high-fat meal. Rozzerem should be taken within 30 minutes before going to bed and activities confined to preparing for bed. The most common adverse events seen with Rozzerem that had at least a 2% incidence difference from placebo were somnolence, dizziness, and fatigue.

Please see adjacent Brief Summary of Prescribing Information.

Please visit www.rozerem.com

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ROZEREM (ramelteon) Tablets

INDICATIONS AND USAGE

ROZEREM (ramelteon) Tablets are indicated for the treatment of insomnia characterized by difficulty initiating and maintaining sleep and early-morning wakening with residual daytime somnolence.

CONTRAINDICATIONS

ROZEREM is contraindicated in patients with a hypersensitivity to ramelteon or any components of the ROZEREM formulation.

WARNINGS

Sleep-related or sleep-disordered breathing disturbances may be present in the absence of clinical symptoms. ROZEREM may increase respiratory resistance in patients with sleep-related breathing disorders, resulting in hypoventilation or apneas, which could result in death. ROZEREM should be used with caution in patients who have a history of sleep-related breathing disorders, or in the presence of a respiratory infection or other conditions that may affect respiratory function. ROZEREM is contraindicated in patients with sleep-related breathing disorders who are unable to maintain an adequate respiratory effort.

PREGNANCY

Pregnancy Category C

ROZEREM has not been studied in humans or animals with the exception of administration of ramelteon to nonhuman primates. ROZEREM should not be used in breastfeeding women because it is not known whether the drug is excreted in human milk. No clinical studies have been conducted in breastfeeding women; however, it is not known whether ramelteon is excreted in human milk. The decision to breastfeed should be based on consideration of the importance of the drug to the mother. It is not known whether ramelteon is excreted in milk from lactating rats. No clinical studies have been conducted in lactating rats; however, ramelteon is not excreted in rhesus monkey milk. Ramelteon is not excreted in dog milk.

ROZEREM AUC in nonhuman primates was similar to the AUC in humans. In a study in which ramelteon was given intravenously in female rhesus monkeys at 300 mg/kg/day, ramelteon was detected in milk for up to 5 days after the last dose. Ramelteon plasma concentrations in milk were approximately one-third of the plasma concentrations in the maternal plasma. Ramelteon was not detected in milk from lactating rats. Therefore, ramelteon is not excreted in human milk.

ROZEREM has not been studied in pregnant or nursing women. It is not known whether ramelteon is excreted in human milk or if it is excreted in milk from lactating rats. No clinical studies have been conducted in lactating rats; however, ramelteon is not excreted in dog milk.

ROZEREM is not excreted in human milk. The decision to breastfeed should be based on consideration of the importance of the drug to the mother. It is not known whether ramelteon is excreted in milk from lactating rats. No clinical studies have been conducted in lactating rats; however, ramelteon is not excreted in dog milk. Therefore, it is not known whether ramelteon is excreted in human milk.

The effects of ramelteon on embryo-fetal development were assessed in nonhuman primates. In a study in which ramelteon was given intravenously to female rhesus monkeys at 300 mg/kg/day, ramelteon was detected in milk for up to 5 days after the last dose. Ramelteon plasma concentrations in milk were approximately one-third of the plasma concentrations in the maternal plasma. Ramelteon was not detected in milk from lactating rats. Therefore, ramelteon is not excreted in human milk.

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NUCLEAR MEDICINE

ROZEREM should not be used in breastfeeding women because it is not known whether the drug is excreted in human milk. No clinical studies have been conducted in breastfeeding women; however, it is not known whether ramelteon is excreted in human milk. The decision to breastfeed should be based on consideration of the importance of the drug to the mother. It is not known whether ramelteon is excreted in milk from lactating rats. No clinical studies have been conducted in lactating rats; however, ramelteon is not excreted in dog milk. Therefore, it is not known whether ramelteon is excreted in human milk.

ADVERSE REACTIONS

The incidence of adverse events was similar between placebo and ROZEREM 32 mg and 64 mg. The incidence of adverse events reported in the Phase 1 through 3 trials was similar between ROZEREM and placebo. The incidence of adverse events during the Phase 1 through 3 trials was similar between ROZEREM and placebo. The incidence of adverse events during the Phase 1 through 3 trials was similar between ROZEREM and placebo.

OVERDOSAGE

ROZEREM has not been studied in animals with the exception of administration of ramelteon to nonhuman primates. ROZEREM should not be used in breastfeeding women because it is not known whether the drug is excreted in human milk. No clinical studies have been conducted in breastfeeding women; however, it is not known whether ramelteon is excreted in human milk. The decision to breastfeed should be based on consideration of the importance of the drug to the mother. It is not known whether ramelteon is excreted in milk from lactating rats. No clinical studies have been conducted in lactating rats; however, ramelteon is not excreted in dog milk. Therefore, it is not known whether ramelteon is excreted in human milk.

ADVERSE REACTIONS

The incidence of adverse events reported in the Phase 1 through 3 trials was similar between ROZEREM and placebo. The incidence of adverse events during the Phase 1 through 3 trials was similar between ROZEREM and placebo. The incidence of adverse events during the Phase 1 through 3 trials was similar between ROZEREM and placebo.

REFERENCES


