

## When child can't sleep, start by treating the parents

Educated parents can change  
sleep-wake behaviors of toddlers to teens

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**S**leep problems are very common in children but more complicated to manage than in adults. That's because you usually must consider the parents' opinions in making the child's diagnosis and change the parents' behavior for the treatment to succeed.

This article describes sleep disorders of children and adolescents, the most effective behavioral therapies, and the limited situations when hypnotic therapy may be appropriate.

### A SYMPTOM, NOT A DIAGNOSIS

Pediatric insomnia is significant difficulty in initiating and/or maintaining sleep that impairs a child's or caregiver's daytime function (*Table 1, page 22*).<sup>1-4</sup> Childhood sleep disorders may manifest primarily as daytime sleepiness and neurobe-



c/o Veer

havioral symptoms or occur with comorbid psychiatric diagnoses such as depression, anxiety, or attention-deficit/hyperactivity disorder (ADHD).

It is important to view insomnia as a symptom—not a diagnosis. Causes of insomnia in children may be medical (drug-related, pain-induced,



Table 1

### Insomnia's negative effects on children and adolescents

Problem	Manifestations
<b>Daytime sleepiness</b>	Yawning, rubbing eyes, resting head on desk
<b>Neurocognitive dysfunction</b>	Decreased cognitive flexibility and verbal creativity Poor abstract reasoning Impaired motor skills Decreased attention and vigilance Memory impairment
<b>Externalizing behaviors</b>	Increased impulsivity, hyperactivity, and aggressiveness
<b>Mood dysregulation</b>	Increased irritability Decreased positive mood Poor affect modulation

Source: References 1-4

or obstructive sleep apnea syndrome), behavioral (poor sleep hygiene or negative sleep-onset associations), or multiple factors (Table 2, page 28).

**Sleep hygiene.** Before starting therapy, educate parents and children about normal sleep development and sleep hygiene, which includes:

- environmental factors (temperature, noise, ambient light)
- scheduling (regular sleep-wake schedule)
- sleep practice (bedtime routine)
- physiologic factors (exercise, timing of meals, caffeine intake).

**Four mechanisms** account for most pediatric sleep disturbances:

- insufficient sleep for individual physiologic needs (“lifestyle” sleep restriction, delayed sleep onset related to behavioral insomnia)
- adequate sleep but fragmented or disrupted by conditions such as obstructive sleep apnea or periodic limb movement disorder that cause frequent or prolonged arousals
- primary disorders of excessive daytime

sleepiness such as narcolepsy (less common than in adults but under-recognized in children and adolescents)

- circadian rhythm disorders in which sleep is usually normal in structure and duration but occurs at an undesired time (delayed sleep phase syndrome).

For practical purposes, sleep disorders also may be defined as primarily behavioral or organic/medical. These two types often are influenced by similar psychosocial and physical/environmental factors and frequently coexist.

### WITH PSYCHIATRIC DISORDERS

Sleep disturbances can profoundly affect the clinical presentation, severity, and management of psychiatric disorders in children and adolescents.<sup>5-7</sup> Up to 75% of children with a major depressive disorder have insomnia (severe in 30%), and one-third of depressed adolescents have delayed sleep-onset. Sleep complaints—especially bedtime resistance, refusal to sleep

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(Simpson-Angus Scale total score >3) or akathisia (Barnes Akathisia global score ≥2). In the same trial, only akathisia events (spontaneously reported COSTART terms akathisia and hyperkinesia) showed a statistically significantly greater adverse events incidence with the 2 higher doses of olanzapine than with placebo. The incidence of patients reporting any extrapyramidal event was significantly greater than placebo only with the highest dose of oral olanzapine (15+2.5 mg/d). In controlled clinical trials of intramuscular olanzapine for injection, there were no statistically significant differences from placebo in occurrence of any treatment-emergent extrapyramidal symptoms, assessed by either rating scales incidence or spontaneously reported adverse events.

**Other Adverse Events**—Dose-relatedness of adverse events was assessed using data from a clinical trial involving 3 fixed oral dosage ranges compared with placebo. The following treatment-emergent events showed a statistically significant trend: asthenia, dry mouth, nausea, somnolence, tremor.

**Vital Sign Changes**—Oral olanzapine was associated with orthostatic hypotension and tachycardia in clinical trials. Intramuscular olanzapine for injection was associated with bradycardia, hypotension, and tachycardia in clinical trials (see PRECAUTIONS).

**Weight Gain**—In placebo-controlled 6-week schizophrenia studies, weight gain was reported in 5.6% of oral olanzapine patients (average 2.8-kg gain) compared to 0.8% of placebo patients (average 0.4-kg loss); 29% of olanzapine patients gained >7% of their baseline weight, compared to 3% of placebo patients. During continuation therapy (238 median days of exposure), 56% of patients met the criterion for having gained >7% of their baseline weight. Average gain during long-term therapy was 5.4 kg.

**Laboratory Changes**—Olanzapine is associated with asymptomatic increases in SGPT, SGOT, and GGT and with increases in serum prolactin and CPK (see PRECAUTIONS). Asymptomatic elevation of eosinophils was reported in 0.3% of olanzapine patients in premarketing trials. There was no indication of a risk of clinically significant neutropenia associated with olanzapine in the premarketing database.

In clinical trials among olanzapine-treated patients with baseline random triglyceride levels of <150 mg/dL (N=659), 0.5% experienced triglyceride levels of ≥500 mg/dL anytime during the trials. In these same trials, olanzapine-treated patients (N=1185) had a mean triglyceride increase of 20 mg/dL from a mean baseline of 175 mg/dL. In placebo-controlled trials, olanzapine-treated patients with baseline random cholesterol levels of <200 mg/dL (N=1034) experienced cholesterol levels of ≥240 mg/dL anytime during the trials more often than placebo-treated patients (N=602; 3.6% vs 2.2% respectively). In these same trials, olanzapine-treated patients (N=2528) had a mean increase of 0.4 mg/dL in cholesterol from a mean baseline of 203 mg/dL, which was significantly different compared to placebo-treated patients (N=1415) with a mean decrease of 4.6 mg/dL from a mean baseline of 203 mg/dL.

**ECG Changes**—Analyses of pooled placebo-controlled trials revealed no statistically significant olanzapine/placebo differences in incidence of potentially important changes in ECG parameters, including QT, QTc, and PR intervals. Olanzapine was associated with a mean increase in heart rate of 2.4 BPM compared to no change among placebo patients.

**Other Adverse Events Observed During Clinical Trials**—The following treatment-emergent events were reported with oral olanzapine at multiple doses ≥1 mg/d in clinical trials (8661 patients, 4165 patient-years of exposure). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. **Frequent** events occurred in ≥1/100 patients; **infrequent** events occurred in 1/100 to 1/1000 patients; **rare** events occurred in <1/1000 patients. **Body as a Whole**—**Frequent**: dental pain, flu syndrome; **Infrequent**: abdomen enlarged, chills, face edema, intentional injury, malaise, moniliasis, neck pain, neck rigidity, pelvic pain, photosensitivity reaction, suicide attempt; **Rare**: chills and fever, hangover effect, sudden death. **Cardiovascular**—**Frequent**: hypotension; **Infrequent**: atrial fibrillation, bradycardia, cerebrovascular accident, congestive heart failure, heart arrest, hemorrhage, migraine, pallor, palpitation, vasodilatation, ventricular extrasystoles; **Rare**: arteritis, heart failure, pulmonary embolus. **Digestive**—**Frequent**: flatulence, increased salivation, thirst; **Infrequent**: dysphagia, esophagitis, fecal impaction, fecal incontinence, gastritis, gastroenteritis, gingivitis, hepatitis, melena, mouth ulceration, nausea and vomiting, oral moniliasis, periodontal abscess, rectal hemorrhage, stomatitis, tongue edema, tooth caries; **Rare**: aphthous stomatitis, enteritis, eructation, esophageal ulcer, glossitis, ileus, intestinal obstruction, liver fatty deposit, tongue discoloration. **Endocrine**—**Infrequent**: diabetes mellitus; **Rare**: diabetic acidosis, goiter. **Hemic and Lymphatic**—**Infrequent**: anemia, cyanosis, leukocytosis, leukopenia, lymphadenopathy, thrombocytopenia; **Rare**: normocytic anemia, thrombocytopenia. **Metabolic and Nutritional**—**Infrequent**: acidosis, alkaline phosphatase increased, bilirubinemia, dehydration, hypercholesterolemia, hyperglycemia, hyperlipemia, hyperuricemia, hypoglycemia, hypokalemia, hyponatremia, lower extremity edema, upper extremity edema; **Rare**: gout, hyperkalemia, hypernatremia, hypoproteinemia, ketosis, water intoxication. **Musculoskeletal**—**Frequent**: joint stiffness, twitching; **Infrequent**: arthritis, arthrosis, leg cramps, myasthenia; **Rare**: bone pain, bursitis, myopathy, osteoporosis, rheumatoid arthritis. **Nervous System**—**Frequent**: abnormal dreams, amnesia, delusions, emotional lability, euphoria, manic reaction, paresthesia, schizophrenic reaction; **Infrequent**: akinesia, alcohol misuse, antisocial reaction, ataxia, CNS stimulation, cogwheel rigidity, delirium, dementia, depersonalization, dysarthria, facial paralysis, hypesthesia, hypokinesia, hypokinesia, incoordination, libido decreased, libido increased, obsessive compulsive symptoms, phobias, somatization, stimulant misuse, stupor, stuttering, tardive dyskinesia, vertigo, withdrawal syndrome; **Rare**: circumoral paresthesia, coma, encephalopathy, neuralgia, neuropathy, nystagmus, paralysis, subarachnoid hemorrhage, tobacco misuse. **Respiratory**—**Frequent**: dyspnea; **Infrequent**: apnea, asthma, epistaxis, hemoptysis, hyperventilation, hypoxia, laryngitis, voice alteration; **Rare**: atelectasis, hiccup, hypoventilation, lung edema, stridor. **Skin and Appendages**—**Frequent**: sweating; **Infrequent**: alopecia, contact dermatitis, dry skin, eczema, maculopapular rash, pruritus, seborrhea, skin discoloration, skin ulcer, urticaria, vesiculobullous rash; **Rare**: hirsutism, pustular rash. **Special Senses**—**Frequent**: conjunctivitis; **Infrequent**: abnormality of accommodation, blepharitis, cataract, deafness, diplopia, dry eyes, ear pain, eye hemorrhage, eye inflammation, eye pain, ocular muscle abnormality, taste perversion, tinnitus; **Rare**: corneal lesion, glaucoma, keratoconjunctivitis, macular hypopigmentation, miosis, mydriasis, pigment deposits lens. **Urogenital**—**Frequent**: vaginitis; **Infrequent**: abnormal ejaculation, amenorrhea, breast pain, cystitis, decreased menstruation, dysuria, female lactation, glycosuria, gynecomastia, hematuria, impotence, increased menstruation, menorrhagia, metrorrhagia, polyuria, premenstrual syndrome, pyuria, urinary frequency, urinary retention, urinary urgency, urination impaired, uterine fibroids enlarged, vaginal hemorrhage; **Rare**: albuminuria, breast enlargement, mastitis, oliguria. (\*Adjusted for gender.)

The following treatment-emergent events were reported with intramuscular olanzapine for injection at one or more doses ≥2.5 mg/injection in clinical trials (722 patients). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. **Body as a Whole**—**Frequent**: injection site pain; **Infrequent**: abdominal pain, fever. **Cardiovascular**—**Infrequent**: AV block, heart block, syncope. **Digestive**—**Infrequent**: diarrhea, nausea. **Hemic and Lymphatic**—**Infrequent**: anemia. **Metabolic and Nutritional**—**Infrequent**: creatine phosphokinase increased, dehydration, hyperkalemia. **Musculoskeletal**—**Infrequent**: twitching. **Nervous System**—**Infrequent**: abnormal gait, akathisia, articulation impairment, confusion, emotional lability. **Skin and Appendages**—**Infrequent**: sweating.

**Postintroduction Reports**—Reported since market introduction and temporally (not necessarily causally) related to olanzapine therapy: allergic reaction (eg, anaphylactoid reaction, angioedema, pruritus or urticaria), diabetic coma, pancreatitis, priapism, rhabdomyolysis, and venous thromboembolic events (including pulmonary embolism and deep venous thrombosis). Random cholesterol levels of ≥240 mg/dL and random triglyceride levels of ≥1000 mg/dL have been rarely reported.

**DRUG ABUSE AND DEPENDENCE**: Olanzapine is not a controlled substance.

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alone, increased nighttime fears, and nightmares—are also common in anxious children and those who have experienced severe trauma (including physical and sexual abuse).

Growing evidence suggests that pediatric “primary” insomnia with no concurrent psychiatric disorder is a risk factor for developing psychiatric conditions later in life—particularly depressive and anxiety disorders. Psychotropics such as psychostimulants and antidepressants also may interfere with sleep.

**ADHD.** Parents often report that children with ADHD have sleep disturbances, especially difficulty initiating sleep, poor sleep quality, restless sleep, frequent nighttime arousals, and shortened sleep duration.<sup>8</sup> Parental observations notwithstanding, most objective methods of examining sleep and sleep architecture (polysomnography, actigraphy) have shown few or inconsistent differences between children with ADHD and controls.

Sleep problems in children with ADHD are often multifactorial. Potential causes include:

- psychostimulant-mediated sleep-onset delay
- bedtime resistance related to comorbid anxiety, oppositional defiant disorder, or circadian phase delay
- settling difficulties related to deficits in sensory integration associated with ADHD.

Adjusting a psychostimulant’s dosing schedule to an earlier time may help children who have trouble falling asleep. In some children, however, sleep-onset delay is caused not by a stimulatory effect but by the medication wearing off at bedtime. A late-day psychostimulant dose might prevent this “rebound.”

When managing a child with ADHD, evaluate comorbid sleep problems and provide diagnostically driven behavioral and/or drug therapy.

## BEHAVIORAL INSOMNIA OF CHILDHOOD

Behavioral insomnia of childhood may manifest as sleep-onset association and limit-setting types.<sup>9</sup>

continued



Table 2

### Diagnostic types of pediatric insomnia

Diagnosis	Characteristics
<b>Behavioral insomnia of childhood</b>	Learned behaviors that interfere with sleep onset or maintenance
Sleep-onset association	Prolonged nighttime arousals because child can fall asleep only with certain sleep associations, such as being soothed by parent
Limit-setting subtype	Active resistance, verbal protests, and repeated demands by child at bedtime
<b>Psychophysiologic insomnia</b>	Conditioned anxiety about sleep difficulty heightens physiologic and emotional arousal, further compromising ability to sleep
Delayed sleep phase disorder	Common in adolescents; persistent phase shift in sleep-wake schedule (later bedtime and wake time) that conflicts with school and lifestyle demands
<b>Secondary insomnia</b>	Not primary; related to other diagnoses or factors
Psychiatric disorders	Depression, anxiety, posttraumatic stress disorder, attention-deficit/hyperactivity disorder
Medical disorders	Obstructive sleep apnea syndrome, pain
Medication	Psychostimulants used to treat ADHD and antidepressants used for major depression may cause sleep-onset delay

The two often coexist, and many children present with both bedtime delays and nighttime arousals. **Sleep-onset association type.** The presenting problem is usually prolonged nighttime arousals resulting in insufficient sleep. The child has learned to fall asleep only with sleep associations, such as being soothed by a parent, that usually are available at bedtime.

During the night, when the child experiences the type of brief arousal that normally occurs at the end of each sleep cycle (every 60 to 90 minutes) or awakens for other reasons, he is unable to get back to sleep (“self-soothe”) unless those same conditions are available to him. The child then “signals” the caregiver by crying (or coming

into the parents’ bedroom) until the necessary associations are provided.

**Limit-setting type** is characterized by active resistance, verbal protests, and repeated demands at bedtime (“curtain calls”) rather than nighttime arousals. If sufficiently prolonged, the sleep-onset delay may result in inadequate sleep duration.

Sometimes bedtime resistance is related to:

- an underlying problem (a medical condition such as asthma or medication use, a sleep disorder such as restless legs, or anxiety)
- a mismatch between the child’s intrinsic circadian preferences (“night owl”) and parental expectations.

Table 3

### 3 treatments for behavioral insomnia of childhood

Treatment	Definition/examples
<b>Extinction</b>	Withdrawing parental assistance at sleep onset and during the night ('systematic ignoring')
<b>Graduated extinction</b>	Gradual rather than abrupt extinction treatment <b>For toddlers</b> , parents check child briefly at successively longer intervals during wake-sleep transition <b>For older children</b> , parents introduce transitional sleep association objects (a blanket or toy) and use positive reinforcement (stickers for remaining in bed)
<b>Preventive parental education</b>	Parents must consistently use behavioral treatment strategies to avoid reinforcing the child's nighttime arousals

Usually, however, this disorder—most common in preschool and older children—develops from a caregiver's inability or unwillingness to set consistent bedtime rules and enforce a regular bedtime. The child's oppositional behavior worsens the problem.

**Behavioral therapy** can alleviate bedtime resistance and nighttime arousals in young children.<sup>10</sup> Controlled group studies strongly support three techniques: unmodified extinction, graduated extinction, and preventive parental education (Table 3).

To use graduated extinction, tell parents to ignore bedtime crying and tantrums for specified periods before checking. Tailor the duration or interval between check-ins to the child's age and temperament; the limiting factor is how much crying the parents can tolerate, as checking is often more to reassure them than the child.

For younger children, parents might check every 2 minutes initially, then gradually lengthen to 5-, 10-, and 15-minute intervals. A common scenario is to double the time between each successive check-in (2 minutes, 4 minutes, 8 min-

utes, etc.). For older children, checking could start at 5- or 10-minute intervals.

During check-ins, the parents briefly comfort the child (usually 15 seconds to 1 minute). Advise parents to minimize interactions that may reinforce the child's attention-seeking behavior.

**To treat limit-setting sleep problems**, recommend a combination of:

- decreased parental attention to bedtime-delaying behavior
- establishing a consistent bedtime routine that does not include stimulating activities such as television viewing
- bedtime "fading" (temporarily setting bedtime to the current sleep-onset time and then gradually advancing bedtime)
- positive reinforcement (sticker charts) for appropriate behavior at bedtime.

Self-relaxation techniques and cognitive-behavioral strategies may help older children.

Behavioral treatment strategies require parental consistency to avoid inadvertently reinforcing nighttime arousals. Warn parents that children's protests frequently escalate temporarily as treatment begins ("postextinction burst").

continued



How parents define a sleep “problem” and how well they accept your treatment recommendations can depend on their cultural values and beliefs about sleep’s meaning, importance, and role in daily life. Family attitudes vary about solitary sleep versus co-sleeping and about offering children transitional objects such as a blanket or toy to help them sleep.

Parents who repeatedly fail to start or enforce behavioral management may have other issues to address, such as depression or marital conflict.

**PSYCHOPHYSIOLOGIC INSOMNIA**

Psychophysiologic insomnia (sleep onset and/or maintenance) occurs primarily in older children and adolescents and results from:

- predisposing factors (genetic vulnerability, underlying medical or psychiatric conditions)
- precipitating factors (acute stress)
- perpetuating factors (poor sleep habits, caffeine use, maladaptive thoughts about sleep).

Conditioned anxiety about difficulty falling asleep or staying asleep heightens physiologic and emotional arousal, further compromising ability to sleep.<sup>11</sup> Educate the patient about sleep hygiene, including:

- using the bed only for sleep
- getting out of bed if unable to fall asleep (stimulus control)
- restricting time in bed to actual time asleep (sleep restriction)
- learning relaxation techniques to reduce anxiety.

**Delayed sleep phase syndrome.** Some youths presenting with sleep-initiation insomnia—particularly adolescents—may have a circadian-based sleep disorder called delayed sleep phase syn-

drome (DSPS). DSPS is a significant, persistent phase shift in the sleep-wake schedule (later bedtime and wake time) that conflicts with the individual’s school, work, or lifestyle demands.<sup>12</sup> The problem is the timing rather than quality of sleep.

Sleep quantity may be compromised if the individual must arise before obtaining adequate sleep. Sleep-onset delays resolve, however, when the patient is allowed to follow his or her preferred later bedtime and wake time.

The typical DSPS sleep-wake pattern is a consistently preferred bedtime/sleep-onset time after midnight and wake time after 10 AM on weekdays and weekends. Adolescents with DSPS often complain of sleep-onset insomnia, extreme difficulty waking in the morning, and profound daytime sleepiness.

A 1- to 2-hour phase shift to a later bedtime and wake time is part of normal pubertal development and has been cited as a rationale for delaying high school start times. The phase shift in DSPS is typically much more dramatic and intractable than the norm.

Treatment options for DSPS include:

- strict sleep-wake schedule (such as 9:30 or 10 PM to 6:30 AM on school nights, with no more than a 1-hour discrepancy on non-school nights)
- melatonin, 3 to 5 mg, given 3 to 4 hours before the desired bedtime, if sleep schedule strategies are unsuccessful
- bright-light therapy in the morning to suppress melatonin secretion and “reset” the body clock, especially if morning waking is particularly difficult.<sup>13</sup>

Teens with a severely delayed sleep phase (>3 to 4 hours) may benefit from chronotherapy. Delay bedtime (“lights out”) and wake times successively—by 2 to 3 hours per day—over several days. For example, if the teen’s preferred fall-

Parents who fail to enforce behavioral management may have depression or marital conflict

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vasodilatation, thinking abnormal, decreased libido, and sweating. **Commonly Observed Adverse Events in Controlled Clinical Trials for MDD, GAD, SAD, and PD—Body as a Whole:** asthenia, headache, flu syndrome, accidental injury, abdominal pain. **Cardiovascular:** vasodilatation, hypertension, palpitation. **Digestive:** nausea, constipation, anorexia, vomiting, flatulence, diarrhea, eructation. **Metabolic/Nutritional:** weight loss. **Nervous System:** dizziness, somnolence, insomnia, dry mouth, nervousness, abnormal dreams, tremor, depression, hypertonia, paresthesia, libido decreased, agitation, anxiety, twitching. **Respiratory System:** pharyngitis, yawn, sinusitis. **Skin:** sweating. **Special Senses:** abnormal vision. **Urogenital System:** abnormal ejaculation, impotence, orgasmic dysfunction (including anorgasmia) in females. **Vital Sign Changes:** Effexor XR was associated with a mean increase in pulse rate of about 2 beats/min in depression and GAD trials and a mean increase in pulse rate of 4 beats/min in SAD trials. (See **WARNINGS—Sustained Hypertension**). **Laboratory Changes:** Clinically relevant increases in serum cholesterol were noted in Effexor XR clinical trials. Increases were duration dependent over the study period and tended to be greater with higher doses. **Other Events Observed During the Premarketing Evaluation of Effexor and Effexor XR—N=6,670.** "Frequent"—events occurring in at least 1/100 patients; "infrequent"—1/100 to 1/1000 patients; "rare"—fewer than 1/1000 patients. **Body 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: appendicitis, bacteremia, carcinoma, cellulitis. **Cardiovascular system** - Frequent: migraine, postural hypotension, tachycardia; Infrequent: angina pectoris, arrhythmia, extrasystoles, hypotension, peripheral vascular disorder (mainly cold feet and/or cold hands), syncope, thrombophlebitis; Rare: aortic aneurysm, arteritis, first-degree atrioventricular block, bigeminy, bundle branch block, capillary fragility, cerebral ischemia, coronary artery disease, congestive heart failure, heart arrest, hematoma, cardiovascular disorder (mitral valve and circulatory disturbance), mucocutaneous hemorrhage, myocardial infarct, pallor, sinus arrhythmia. **Digestive system** - Frequent: increased appetite; Infrequent: bruxism, colitis, dysphagia, tongue edema, esophagitis, gastritis, gastroenteritis, gastrointestinal ulcer, gingivitis, glossitis, rectal hemorrhage, hemorrhoids, melena, oral moniliasis, stomatitis, mouth ulceration; Rare: abdominal distension, biliary pain, cheilitis, cholecystitis, cholelithiasis, esophageal spasms, duodenitis, hematemesis, gastroesophageal reflux disease, gastrointestinal hemorrhage, gum hemorrhage, hepatitis, ileitis, jaundice, intestinal obstruction, liver tenderness, parotitis, periodontitis, proctitis, rectal disorder, salivary gland enlargement, increased salivation, soft stools, tongue discoloration. **Endocrine system** - Rare: galactorrhea, goiter, hyperthyroidism, hypothyroidism, thyroid nodule, thyroiditis. **Hemic and lymphatic system** - Frequent: ecchymosis; Infrequent: anemia, leukocytosis, leukopenia, lymphadenopathy, thrombocytopenia; Rare: basophilia, bleeding time increased, cyanosis, eosinophilia, lymphocytosis, multiple myeloma, purpura, thrombocytopenia. **Metabolic and nutritional** - Frequent: edema, weight gain; Infrequent: alkaline phosphatase increased, dehydration, hypercholesterolemia, hyperglycemia, hyperlipidemia, hypoglycemia, hypokalemia, SGOT increased, SGPT increased, thirst; Rare: alcohol intolerance, bilirubinemia, BUN increased, creatinine increased, diabetes mellitus, glycosuria, gout, healing abnormal, hemochromatosis, hypercalcinuria, hyperkalemia, hyperphosphatemia, hyperuricemia, hypochlosterolemia, hyponatremia, hypophosphatemia, hypoproteinemia, uremia. **Musculoskeletal system** - Frequent: arthralgia; Infrequent: arthritis, arthrosis, bone spurs, bursitis, leg cramps, myasthenia, tenosynovitis; Rare: bone pain, pathological fracture, muscle cramp, muscle spasms, musculoskeletal stiffness, myopathy, osteoporosis, osteosclerosis, plantar fasciitis, rheumatoid arthritis, tendon rupture. **Nervous system** - Frequent: amnesia, confusion, depersonalization, hyposthesia, thinking abnormal, trismus, vertigo; Infrequent: akathisia, apathy, ataxia, circumoral paresthesia, CNS stimulation, emotional lability, euphoria, hallucinations, hostility, hyperesthesia, hyperkinesia, hypotonia, incoordination, manic reaction, myoclonus, neuralgia, neuropathy, psychosis, seizure, abnormal speech, stupor, suicidal ideation; Rare: abnormal/changed behavior, adjustment disorder, akinesia, alcohol abuse, aphasia, bradykinesia, buccoglossal syndrome, cerebrovascular accident, feeling drunk, loss of consciousness, delusions, dementia, dystonia, energy increased, facial paralysis, abnormal gait, Guillain-Barré syndrome, homicidal ideation, hyperchlorhydria, hypokinesia, hysteria, impulse control difficulties, libido increased, motion sickness, neuritis, nystagmus, paranoid reaction, paresis, psychotic depression, reflexes decreased, reflexes increased, toricollis. **Respiratory system** - Frequent: cough increased, dyspnea; Infrequent: asthma, chest congestion, epistaxis, hyperventilation, laryngismus, laryngitis, pneumonia, voice alteration; Rare: atelectasis, hemoptysis, hypoventilation, hypoxia, larynx edema, pleurisy, pulmonary embolus, sleep apnea. **Skin and appendages** - Frequent: pruritus; Infrequent: acne, alopecia, contact dermatitis, dry skin, eczema, maculopapular rash, psoriasis, urticaria; Rare: brittle nails, erythema nodosum, exfoliative dermatitis, lichenoid dermatitis, hair discoloration, skin discoloration, furunculosis, hirsutism, leukoderma, miliaria, petechial rash, pruritic rash, pustular rash, vesiculobullous rash, seborrhea, skin atrophy, skin hypertrophy, skin striae, sweating decreased. **Special senses** - Frequent: abnormality of accommodation, mydriasis, taste perversion; Infrequent: conjunctivitis, diplopia, dry eyes, eye pain, hyperacusis, otitis media, parosmia, photophobia, taste loss, visual field defect; Rare: blepharitis, cataract, chromatopsia, conjunctival edema, corneal lesion, deafness, exophthalmos, eye hemorrhage, glaucoma, retinal hemorrhage, subconjunctival hemorrhage, keratitis, labyrinthitis, miosis, papilledema, decreased pupillary reflex, otitis externa, scleritis, uveitis. **Urogenital system** - Frequent: prostatic disorder (prostatitis, enlarged prostate, and prostate irritability), urination impaired; Infrequent: albuminuria, amenorrhea, breast pain, cystitis, dysuria, hematuria, kidney calculus, kidney pain, leukorrhea, menorrhagia, metrorrhagia, nocturia, polyuria, pyuria, urinary incontinence, urinary retention, urinary urgency, vaginal hemorrhage, vaginitis; Rare: abortion, anuria, balanitis, bladder pain, breast discharge, breast engorgement, breast enlargement, endometriosis, female lactation, fibrocystic breast, calcium crystalluria, cervicitis, orchitis, ovarian cyst, prolonged erection, gynecostasia (male), hypomenorrhea, kidney function abnormal, mastitis, menopause, pyelonephritis, oliguria, salpingitis, urolithiasis, uterine hemorrhage, uterine spasm, vaginal dryness. **Postmarketing Reports:** agranulocytosis, anaphylaxis, aplastic anemia, catatonia, congenital anomalies, CPK increased, deep vein thrombophlebitis, delirium, EKG abnormalities such as QT prolongation; cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia, ventricular extrasystoles, and rare reports of ventricular fibrillation and ventricular tachycardia, including torsades de pointes; epidermal necrosis/Stevens-Johnson syndrome, erythema multiforme, extrapyramidal symptoms (including dyskinesia and tardive dyskinesia), angle-closure glaucoma, hemorrhage (including eye and gastrointestinal bleeding), hepatic events (including GGT elevation; abnormalities of unspecified liver function tests; liver damage, necrosis, or failure; and fatty liver), involuntary movements, LDH increased, neuroleptic malignant syndrome-like events (including a case of a 10-year-old who may have been taking methylphenidate, was treated and recovered), neutropenia, night sweats, pancreatitis, pancytopenia, panic, prolactin increased, pulmonary eosinophilia, renal failure, rhabdomyolysis, serotonin syndrome, shock-like electrical sensations or tinnitus (in some cases, subsequent to the discontinuation of venlafaxine or tapering of dose), and SIADH (usually in the elderly). Elevated clozapine levels that were temporally associated with adverse events, including seizures, have been reported following the addition of venlafaxine. Increases in prothrombin time, partial thromboplastin time, or INR have been reported when venlafaxine was given to patients on warfarin therapy. **DRUG ABUSE AND DEPENDENCE:** Effexor XR is not a controlled substance. Evaluate patients carefully for history of drug abuse and observe such patients closely for signs of misuse or abuse. **OVERDOSAGE:** Electrocardiogram changes (e.g., prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, altered level of consciousness (ranging from somnolence to coma), rhabdomyolysis, seizures, vertigo, liver necrosis, and death have been reported. Treatment should consist of those general measures employed in the management of overdose with any antidepressant. Ensure an adequate airway, oxygenation and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Due to the large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for venlafaxine are known. In managing overdose, consider the possibility of multiple drug involvement. Consider contacting a poison control center for additional information on the treatment of overdose. Telephone numbers for certified poison control centers are listed in the Physicians' Desk Reference® (PDR). **DOSE AND ADMINISTRATION:** Consult full prescribing information for dosing instructions. **Switching Patients to or From an MAOI—**At least 14 days should elapse between discontinuation of an MAOI and initiation of therapy with Effexor XR. At least 7 days should be allowed after stopping Effexor XR before starting an MAOI (see **CONTRAINDICATIONS** and **WARNINGS**). This brief summary is based on Effexor XR Prescribing Information W10404C019, revised November 2005.

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asleep time is 3 AM and wake time is noon, then bedtime and wake time would be 5 AM to 2 PM the first day; 7 AM to 4 PM the next day, and so forth until the sleep-onset time coincides with the desired bedtime.

If the adolescent also has school avoidance or a mood disorder—which is often the case—non-compliance with treatment is common. More-intensive behavioral and medication approaches may be needed.

## USE HYPNOTICS?

Most insomnia in children and adolescents can be managed from infancy on with behavior therapy alone. If not, combined behavioral and drug interventions may be appropriate, such as when:

- the family is overwhelmed by the sleep problem and cannot execute behavioral strategies
- the child's safety is at risk (engaging in dangerous activities during night awakenings, for example)
- treating specific populations (such as children with ADHD or autistic disorders).

The decision to prescribe medication for a child with insomnia is based largely on clinical experience, empirical data in adults, and small case series. No medications are FDA-approved for use as hypnotics in children. Sleep aids most commonly prescribed in clinical practice or recommended by pediatric clinicians include:

- antihistamines such as diphenhydramine

Screen for insomnia in every child with mood, learning, or behavioral problems. Consider whether psychiatric comorbidities and medications may be worsening the sleep disorder. Behavioral management is usually effective, without medication. Consider hypnotics in extreme cases or for children with ADHD or autism.

BottomLine  
continued



- tricyclic antidepressants (amitriptyline, trazodone, and others)
- benzodiazepines (clonazepam)
- nonbenzodiazepine hypnotics (zolpidem, zaleplon)
- alpha-agonists (clonidine).<sup>14,15</sup>

Sedating antipsychotics (such as risperidone) and anticonvulsants (divalproex sodium) are sometimes used, such as for children with mental retardation. Sedating antidepressants (such as mirtazapine) may help children with depression and concomitant insomnia.

Use these medications with caution in children, as safety and tolerability are unknown. Prescribe the lowest dosage for the briefest time possible, and use in combination with behavioral management strategies. Choose the shortest-acting agents to avoid morning grogginess. Chloral hydrate and barbiturates are rarely indicated in children because of side effects.

**Over-the-counter products.** Parents often use non-prescription products such as diphenhydramine, melatonin, and herbal preparations to treat children's sleep problems, with or without a clinician's recommendation. Most herbal preparations are generally safe but remain untested in pediatric patients.

Antihistamines such as diphenhydramine are generally well-tolerated, but they may have a paradoxical agitating effect. Tolerance also tends to develop, leading to increasing doses. Parents may inadvertently overdose a child by giving multiple nonprescription products with diphenhydramine as the active ingredient (such as combining Benadryl with Tylenol PM).

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Related resources

- ▶ National Sleep Foundation. Information for patients and clinicians. [www.sleepfoundation.org](http://www.sleepfoundation.org).
- ▶ American Academy of Sleep Medicine. Professional and patient resources and links. [www.aasmnet.org](http://www.aasmnet.org).
- ▶ Mindell J, Owens J. *A clinical guide to pediatric sleep: diagnosis and management of sleep problems in children and adolescents*. Philadelphia: Lippincott Williams and Wilkins; 2003.
- ▶ Owens J, Mindell J. *Take charge of your child's sleep: the all-in-one resource for solving sleep problems in kids and teens*. New York: Marlowe & Co.; 2005.

DRUG BRAND NAMES

- |   |                         |
|---|-------------------------|
| Amitriptyline • Elavil                                  | Mirtazapine • Remeron   |
| Clonazepam • Klonopin                                   | Risperidone • Risperdal |
| Clonidine • Catapres                                    | Trazodone • Desyrel     |
| Diphenhydramine • Benadryl and others (nonprescription) | Zaleplon • Sonata       |
| Divalproex sodium • Depakote                            | Zolpidem • Ambien       |

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