



American Pharmaceutical Association

*The National Professional Society of Pharmacists*

# New Product Bulletin

## *Concerta<sup>TM</sup>* *(extended-release methylphenidate HCl)*

### INSIDE:

**Background Information on Attention Deficit Hyperactivity Disorder and Use of Concerta (extended-release methylphenidate HCl)**

**Answers to Patients' Questions About Attention Deficit Hyperactivity Disorder and Use of Concerta (extended-release methylphenidate HCl)**

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Dear Colleague:

Attention deficit hyperactivity disorder (ADHD) is the most commonly diagnosed psychiatric disorder in children. Many misconceptions surround the disorder and its treatment. For example, ADHD has been attributed incorrectly to poor parenting skills. Also, concerns have been raised about the excessive use and long-term effects of drug therapies commonly prescribed to treat ADHD. Pharmacists can provide information about ADHD and its treatment to parents and caregivers of children with the disorder so that they can weigh the benefits and risks of drug therapy and make informed decisions about the use of medication in their child.

Stimulants are regarded as the most effective treatment for ADHD, and they are the most extensively studied medications for ADHD. Methylphenidate in particular is used widely to treat ADHD. However, until recently, the usefulness of stimulants has been limited by their short duration of action, the need for multiple daily doses, and fluctuations in blood drug levels over the course of a day.

Concerta™ is an extended-release formulation of methylphenidate HCl that was approved recently by the Food and Drug Administration for the treatment of ADHD in patients at least 6 years of age. It uses the OROS® delivery system to provide a prolonged effect, enabling once-daily dosing. This New Product Bulletin provides a comprehensive description of the pharmacokinetics, dosing, administration, efficacy, adverse effects, and cautions associated with the use of Concerta. The prevalence, etiology, diagnosis, and pathophysiology of ADHD also are summarized. Answers to questions commonly asked by parents, caregivers, and patients are provided; these questions and answers may be photocopied for distribution.

We hope that you find this publication useful.

Sincerely yours,

Patricia A. Marken, PharmD, FCCP, BCPP  
Advisory Board Chairperson

## Introduction

Attention deficit hyperactivity disorder (ADHD, sometimes referred to as attention deficit disorder) is a psychiatric disorder characterized by inattention, hyperactivity, or impulsivity (Table 1) that is more frequent or severe than is appropriate for the developmental level.<sup>1</sup> Inattention often results in careless errors in schoolwork or other activities, failure to complete tasks, and avoidance of activities that require sustained mental effort, organization, or concentration. Hyperactivity may manifest as fidgeting and inability to sit still (or restlessness in adults) and noisiness or excessive talkativeness.<sup>1</sup> Impulsivity often is characterized by impatience, difficulty waiting for one's turn, and a tendency to interrupt others. It may result in accidents (e.g., bumping into people or objects).<sup>1</sup>

Symptoms of ADHD manifest before the age of 7 years, according to the diagnostic criteria in Table 1.<sup>1</sup> In most cases, ADHD is diagnosed when a child enters school and has difficulty adjusting to the structured environment.<sup>1,2</sup> The nature and severity of symptoms vary among patients and change over time within an individual.<sup>3</sup> Hyperactivity tends to decrease over time, although inattention changes little.<sup>4</sup>

Attention deficit hyperactivity disorder affects an estimated 3% to 7% of school-aged children.<sup>1</sup> However, estimates vary widely from 1% to 24% because of differences in diagnostic criteria (there is no pathognomonic marker for ADHD).<sup>5-7</sup> ADHD traditionally has been thought of as a disorder that affects schoolchildren, but up to two thirds of children with the disorder continue to have symptoms (albeit fewer or milder ones) in adulthood.<sup>8</sup>

## Epidemiology

Genetics may play a role in ADHD. The risk of ADHD is five to seven times higher in the siblings of a child with ADHD than it is in the general population.<sup>6</sup> Studies involving twins revealed that the risk of ADHD in an identical twin of a child with ADHD is up to 18 times higher than the risk in a nontwin sibling with less similar genes.<sup>6</sup> One in four children with ADHD has a parent with a history of the disorder.<sup>3</sup> One third of fathers who have a history of ADHD have a child affected by the disorder.<sup>7</sup>

ADHD affects boys disproportionately, possibly because of underdiagnosis in girls.<sup>5,9</sup> The prevalence of ADHD in boys is two to nine times higher than that in girls.<sup>1,5,7</sup> In girls, inattention is more likely to predominate than hyperactivity or impulsivity, which may cause the disorder to go unrecognized in girls.<sup>3</sup> Proposed risk factors for ADHD include premature birth; maternal use of alcohol (i.e., fetal alcohol syndrome), tobacco, and drugs (e.g., cocaine); lead poisoning; meningitis; and brain injury.<sup>3,6,10</sup> Dietary factors (e.g., sugar, food additives) are not thought to cause ADHD, although some clinicians find that dietary factors may worsen symptoms.<sup>10,11</sup> The role of diet in ADHD is somewhat controversial.

One in three patients with ADHD has at least one comorbid psychiatric disorder (some patients have more than one comorbid condition).<sup>12</sup> The estimated prevalence of oppositional defiant disorder—a recurrent pattern of negative, defiant, disobedient, and hostile behavior toward authority figures—in conjunction with ADHD is 35% to more than 50%.<sup>1,12,13</sup> As many as half of patients with ADHD are diagnosed with conduct disorder, which is characterized by repeated, persistent behavior in which the basic rights of others or age-appropriate society norms or rules are violated.<sup>12,13</sup> Conduct disorder may manifest as aggression, property destruction, deceitfulness, or theft.<sup>1</sup> The prevalence of comorbid anxiety disorder and depression in patients with ADHD is 10% to 25%.<sup>12,13</sup>

## Consequences

Attention deficit hyperactivity disorder can interfere with intellectual development and is associated with poor performance at school or work, low self-esteem, and conflict with family members, teachers, classmates, and coworkers.<sup>1</sup> An inability to complete schoolwork or other tasks in an appropriate fashion often is perceived as the result of laziness or irresponsibility.<sup>1</sup> Attention deficit hyperactivity disorder can impair interpersonal relationships. Children with ADHD may have difficulty making friends or experience peer rejection because of their impulsive behavior and inability to cooperate in

### Learning Objectives

After reading this article, the pharmacist should be able to:

1. Characterize the etiology, diagnosis, and pathophysiology of attention deficit hyperactivity disorder (ADHD).
2. Discuss the role of nondrug and drug therapies in managing ADHD.
3. Describe the appropriate use of extended-release methylphenidate HCl (Concerta) in the management of ADHD.
4. Counsel patients, parents, and caregivers about the proper use of Concerta and monitor therapeutic response.
5. Answer questions commonly asked by patients, parents, and caregivers about ADHD and the use of Concerta.

Table 1.

## Diagnostic Criteria for Attention Deficit Hyperactivity Disorder

A. Either (1) or (2)

(1) six (or more) of the following symptoms of **inattention** have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

*Inattention*

- often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities
- often has difficulty sustaining attention in tasks or play activities
- often does not seem to listen when spoken to directly
- often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior<sup>a</sup> or failure to understand instructions)
- often has difficulty organizing tasks and activities
- often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)
- often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools)
- is often easily distracted by extraneous stimuli
- is often forgetful in daily activities

(2) six (or more) of the following symptoms of **hyperactivity-impulsivity** have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

*Hyperactivity*

- often fidgets with hands or feet or squirms in seat
- often leaves seat in classroom or in other situations in which remaining seated is expected
- often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
- often has difficulty playing or engaging in leisure activities quietly
- is often "on the go" or often acts as if "driven by a motor"
- often talks excessively

*Impulsivity*

- often blurts out answers before questions have been completed
- often has difficulty awaiting turn
- often interrupts or intrudes on others (e.g., butts into conversations or games)

B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before age 7 years.

C. Some impairment from the symptoms is present in two or more settings (e.g., at school or work and at home).

D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder).

<sup>a</sup>Resisting work or school tasks that require self-application because of an unwillingness to conform to the demands of others is oppositional behavior.

Source: Reprinted with permission from Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR (Text Revision). 4th edition. Copyright 2000, American Psychiatric Association.

group activities.<sup>7,14</sup> Social and emotional development and academic and vocational success can be adversely affected.<sup>14</sup> Injury rates in patients with ADHD are higher than those in the general population.<sup>14</sup>

The direct costs of treating ADHD are substantial and are not always covered by health insurance.<sup>14</sup> Public school expenditures for students with ADHD (e.g., for special education) amounted to an estimated \$3 billion in 1995 (the last year for which data are available).<sup>14</sup>

## Diagnosis

Early recognition and diagnosis of ADHD can provide an opportunity to minimize the impact of the disorder on educational and psychosocial development.<sup>12</sup> Many patients and parents of affected children are relieved to receive the diagnosis of ADHD because it explains the symptoms.<sup>8</sup> However, the benefits of early diagnosis of ADHD must be weighed against the disadvantages of "labeling" a child with the disorder at an early age.

According to the American Academy of Pediatrics, screening for ADHD symptoms can be initiated in children 6 to 12 years of age by primary care providers during routine health visits to increase the likelihood of early detection of ADHD in this age group.<sup>12</sup> Screening involves obtaining a history from parents or caregivers and children, with questions about school performance and behavior problems in the school and home settings. However, the wisdom of screening has been questioned because of the possibility that it could increase the number of false-positive diagnoses.<sup>15</sup>

The actual diagnosis of ADHD should be made by a specialist based on the criteria in Table 1, using information from parents or caregivers, school reports (preferably directly from the classroom teacher), mental health care professionals (if they have been involved), and an interview or examination of the child by a qualified health care professional.<sup>12,16</sup> ADHD-specific questionnaires and rating scales are available to assist in obtaining information from parents or caregivers and teachers.<sup>12</sup>

Brain imaging studies and electroencephalography are not routinely recommended as part of the diagnostic workup for ADHD.

## Pathophysiology

The underlying pathophysiologic changes that cause ADHD are unknown.<sup>17</sup> The disorder is considered to be heterogeneous because ADHD symptoms vary among and within individuals and because the disorder often is accompanied by multiple comorbid conditions. The pathogenesis of ADHD is probably multifactorial, with both neurobiologic and genetic abnormalities.<sup>6,18,19</sup> The disorder is thought to be polygenic (i.e., the result of mutations in multiple genes).<sup>6</sup> Dysregulation of multiple brain neurotransmitters (especially dopamine and norepinephrine) is likely to play a role because essentially all medications that are effective in treating ADHD affect catecholamine transmission, and medications that do not affect catecholamine transmission generally are not effective.<sup>18</sup>

The prefrontal cortex (the area of the cortex behind the forehead) and basal ganglia (clusters of nerve cells located deep within the cerebral hemispheres) are key structures in a complex neural system that regulates attention, motor function, and behavior.<sup>6,18</sup> The cerebellum is involved in motor and nonmotor cognitive tasks and has neural connections with the prefrontal cortex via the thalamus. Brain imaging studies have revealed that the right prefrontal cortex, basal ganglia, and cerebellum are substantially smaller in patients with ADHD than in those without the disorder.<sup>5,6</sup> The small size of the prefrontal cortex and basal ganglia suggests poor connectivity between the two areas, which could in theory interfere with function and cause ADHD symptoms.<sup>18</sup> Some (but not all) studies found that the metabolic rate (i.e., glucose utilization), which correlates with metabolic activity in these areas, is low in patients with ADHD.<sup>7,17,18</sup>

Other brain morphologic abnormalities have been identified in patients with ADHD. A smaller-than-normal posterior parietal cortex, an area that processes visual and spatial information and has recip-

rocal connections with the prefrontal cortex, could interfere with the screening of irrelevant sensory information and contribute to inattention.<sup>18</sup> This morphologic abnormality may be associated with dysfunction of postsynaptic  $\alpha_2$ -adrenergic receptors, which regulate presynaptic norepinephrine release through a negative feedback mechanism.<sup>18</sup> However, norepinephrine dysfunction is not found consistently in children with ADHD.<sup>18</sup>

Genetic mutations that reduce the sensitivity of receptors to dopamine or increase the activity of dopamine transporters that facilitate neuronal reuptake of dopamine have been theorized in patients with ADHD.<sup>6,19,20</sup> Medications that inhibit the dopamine transporter (e.g., methylphenidate, dextroamphetamine, pemoline, bupropion) are effective in treating ADHD.<sup>18</sup>

## Management

Various nonpharmacologic treatment modalities (psychosocial interventions and remedial education) and drug therapies (e.g., stimulants, antidepressants) have been used to treat ADHD. Stimulants (methylphenidate, dextroamphetamine, and pemoline) and psychosocial treatment (e.g., behavioral treatment) are the best-studied modalities. Most studies of stimulants evaluated the efficacy of short-term treatment (up to about 3 months); few data are available for long-term efficacy.<sup>14,21</sup> Studies that have compared stimulants with psychosocial treatment consistently report greater efficacy of stimulants.<sup>14</sup> Using behavioral treatment (e.g., parent training, intensive child-focused treatment) in combination with drug therapy may lead to improved social skills, but the benefit beyond that produced by drug therapy alone is not great.<sup>14,22</sup>

## Pharmacologic Therapy

**Stimulants.** Stimulants (Table 2) are first-line agents for treating ADHD and the only agents approved by the Food and Drug Administration (FDA) for this indication.<sup>26</sup> Methylphenidate, dextroamphetamine, and pemoline have central nervous system (CNS) and respiratory stimulant properties and weak sympathomimetic activity.<sup>23</sup> They promote the release of dopamine and norepinephrine from presynaptic neurons and inhibit the reuptake of these neurotransmitters in the CNS, although the exact mechanism by which stimulants improve ADHD symptoms is unclear.<sup>3,23</sup> Improvement in inattention, hyperactivity, and impulsivity occurs in 70% to 90% of children with ADHD who receive stimulants, once the dosage is adjusted to minimize adverse effects.<sup>23</sup> However, improvement in ADHD symptoms is variable (some symptoms respond better than others) and treatment may not normalize all behavioral problems or improve academic and social skills.<sup>14</sup>

Methylphenidate is the most widely studied and used stimulant in patients with ADHD.<sup>19,27</sup> However, there are few (if any) differences in efficacy among the different stimulants.<sup>14</sup> Failure to respond to one agent does not predict response to other agents.<sup>28</sup>

Table 2.

## Stimulants for Treatment of Attention Deficit Hyperactivity Disorder<sup>a</sup>

Drug (DEA Schedule)	Strengths and Dosage Forms (Brand Name)	Recommended Dosage
Dextroamphetamine sulfate (CII)	5- and 10-mg tablets (Dexedrine, DextroStat); 5-, 10-, 15-mg sustained-release capsules (Dexedrine Spansules); 1.25-, 2.5-, 5-, 7.5-mg tablets in combination with amphetamine aspartate, amphetamine sulfate, and dextroamphetamine saccharate (Adderall)	<i>Age 3–5 yr:</i> 2.5 mg/day initially; then increase by 2.5 mg/day at weekly intervals as needed <sup>b</sup>  <i>Age ≥ 6 yr:</i> 5 mg once or twice daily initially; then increase by 5 mg/day at weekly intervals as needed (rarely to exceed 40 mg/day) <sup>b</sup>
Methylphenidate HCl (CII)	5-, 10-, 20-mg immediate-release tablets (Ritalin); 20-mg sustained-release tablets (Ritalin-SR); 18-, 36-, and 54-mg extended-release tablets (Concerta)	<i>Age ≥ 6 yr:</i> 5 mg as immediate-release tablets twice daily before breakfast and lunch initially; then gradually increase by 5–10 mg/day at weekly intervals, not to exceed 60 mg/day <sup>c</sup>  <i>Adults:</i> 10–60 mg/day (20–30 mg/day is the average effective dosage) as immediate-release tablets in two or three divided doses, preferably 30–45 min before meals <sup>c</sup>
Pemoline (CIV)	18.75-, 37.5-, 75-mg tablets (Cylert); 37.5-mg chewable tablets (Cylert)	<i>Age ≥ 6 yr:</i> 37.5 mg/day as a single daily dose each morning initially, then increase by 18.75 mg/day at weekly intervals as needed (56.25–75 mg/day usually is effective), not to exceed 112.5 mg/day in children

DEA = Drug Enforcement Administration.

<sup>a</sup>All therapies are approved by the Food and Drug Administration for the treatment of attention deficit hyperactivity disorder and are administered orally. Treatment usually should not be continued indefinitely. It should be interrupted occasionally to assess the patient's condition because improvement may be maintained temporarily or permanently after the drug is discontinued.

<sup>b</sup>The dosage listed is for dextroamphetamine sulfate alone or in combination preparations that contain amphetamine aspartate, amphetamine sulfate, and dextroamphetamine saccharate (Adderall). The initial dose should be given on awakening. When the drug is given in divided doses, it should be given at intervals of 4 to 6 hours.

<sup>c</sup>Methylphenidate sustained-release tablets (Ritalin-SR) may be used if the strength corresponds to the 8-hour dosage of immediate-release tablets. The recommended dosage of extended-release methylphenidate HCl (Concerta) is 18 to 54 mg once daily (see Table 3).

Source: References 23–25.

There is considerable variability among individuals in the dose-response relationship, so individualization of the dosage is recommended.<sup>28</sup>

Stimulants have been available in immediate-release and sustained-release dosage forms. (Concerta, a new extended-release formulation of methylphenidate, is described in detail later in this New Product Bulletin.) The duration of action of immediate-release dosage forms typically is short (2 to 6 hours), requiring the use of several daily doses to maintain a therapeutic response.<sup>3</sup> Sustained-release dosage forms with a duration of action of at least 8 hours eliminate the need for medication administration during the school day (an embarrassment for some children that can interfere with patient adherence).<sup>29</sup> However, additional doses of sustained-release formulations may be needed if children participate in after-school activities. Sustained-release dosage forms may have a

slower onset of action and be less effective than immediate-release dosage forms.<sup>3,30,31</sup> Moreover, sustained-release dosage forms may interfere with sleep and cannot be chewed, which is a disadvantage for children who are unable to swallow solid oral dosage forms.<sup>3,29</sup>

Adverse effects from stimulants include nervousness, insomnia, abdominal pain, anorexia, and weight loss.<sup>23,32</sup> These effects usually are dose related, occur early in treatment, and may decrease with continued treatment.<sup>14</sup> Suppression of growth rate may occur, but final height does not appear to be affected.<sup>14</sup> Pemoline has been associated with life-threatening liver failure.<sup>23</sup> Therefore, other stimulants are preferred.

The use of stimulants has been associated with tics, although the tics usually are transient and rarely become chronic.<sup>29</sup> Up to half of patients with Tourette's disorder (an illness characterized by tics) have ADHD.<sup>29</sup> The use of stimulants in patients with motor tics or a

family history or diagnosis of Tourette's syndrome is controversial because although such use generally is contraindicated, ADHD symptoms improve with stimulant therapy in many of these patients.<sup>29</sup>

High doses of stimulants (particularly dextroamphetamine) can cause CNS and cardiovascular damage, hypertension, compulsive behavior, and (rarely) hallucinogenic responses.<sup>14</sup> Leukopenia rarely has been associated with stimulant use.<sup>29</sup> Therefore, complete blood counts are recommended before initiating therapy and annually thereafter until therapy is discontinued.<sup>29</sup>

The abuse potential of stimulants is well known (they are classified as controlled substances by the Drug Enforcement Administration). Data are conflicting as to whether the use of stimulants to treat ADHD increases the risk of abuse of other drugs.<sup>14</sup>

Some clinicians recommend that stimulant therapy be interrupted occasionally (e.g., on weekends or for 4 to 6 weeks every 6 to 12 months) to assess the patient's condition because improvement may be maintained temporarily or permanently after the drug is discontinued.<sup>8,19,33</sup> Such drug "holidays" often are timed to coincide with school breaks or summer vacations, when calm behavior and focused attention usually are not as crucial.<sup>34</sup>

**Antidepressants.** Tricyclic antidepressants (e.g., desipramine, imipramine) have been used to treat ADHD in children (presumably because these agents block neuronal reuptake of norepinephrine and other neurotransmitters).<sup>23,35,36</sup> They are considered second-line treatment for ADHD in patients whose symptoms do not respond to stimulants (tricyclic antidepressants are less effective than stimulants) or who cannot use stimulants because of abuse problems or intolerable adverse effects (e.g., insomnia).<sup>3,36</sup> Tricyclic antidepressants may be helpful when severe depression or anxiety accompanies ADHD.<sup>19</sup> However, tolerance may develop to the therapeutic effect of tricyclic antidepressants.<sup>36</sup> These agents can cause fatigue and sedation (these effects tend to diminish with time), weight gain, constipation, dry mouth, blurred vision, and cardiac arrhythmias.<sup>14,37</sup> Overdosage of tricyclic antidepressants can be fatal.<sup>23</sup>

Bupropion is a weak dopamine agonist.<sup>19</sup> It reduced ADHD symptoms in studies of children with the disorder.<sup>29</sup> The risk of cardiovascular and most anticholinergic adverse effects and weight gain is lower with bupropion than with tricyclic antidepressants.<sup>23</sup> However, bupropion can cause fatigue, agitation, dry mouth, insomnia, headache, tics, rash, nausea, and vomiting.<sup>19</sup> It also increases the risk of seizures.<sup>23</sup>

Selective serotonin reuptake inhibitors potentiate the effect of serotonin in the CNS and have little effect on other neurotransmitters.<sup>23</sup> These agents are not widely used in patients with ADHD because they have inconsistent effects and often worsen symptoms.<sup>35</sup> Venlafaxine, a potent inhibitor of neuronal serotonin and norepinephrine reuptake and a weak inhibitor of dopamine reuptake, has been used with some success in adults with ADHD.<sup>24,38</sup> However, it may aggravate hyperactivity in children and adolescents.<sup>39</sup>

**Clonidine and Guanfacine.** Clonidine and guanfacine stimulate presynaptic  $\alpha_2$ -adrenergic receptors in the CNS, which reduces norepinephrine activity.<sup>23,24</sup> They may be helpful for patients with concomitant tic disorders, aggression, or insomnia (these agents cause sedation).<sup>37,40-42</sup> Clonidine (administered orally or as a transdermal patch) is less effective than stimulants for the treatment of ADHD.<sup>40</sup> The efficacy of guanfacine has not yet been compared directly with that of stimulants. Clonidine has a short half-life (the oral formulation typically is given several times daily) and causes troublesome adverse effects (e.g., hypotension, heart block).<sup>19,23,40</sup> Guanfacine has a longer half-life and may cause less sedation than clonidine.<sup>41</sup>

Abrupt discontinuation of clonidine or guanfacine can lead to a rebound increase in blood pressure and headache, dizziness, agitation, fever, chest pain, sleep disturbance, nausea, and vomiting.<sup>37</sup> Sudden death has been reported when clonidine was used in combination with methylphenidate or dextroamphetamine.<sup>36,43</sup>

## Psychosocial and Educational Interventions

Behavioral strategies for ADHD include contingency management, parent training in child management skills, clinical behavior therapy, and cognitive-behavioral treatment.<sup>14</sup> Contingency management provides reinforcement in accordance with behavior, using a points or token system to encourage good behavior.<sup>19</sup> Parents, teachers, or both are taught how to use the contingency management system as part of clinical behavior therapy.<sup>14,44</sup> Structured settings often are used for behavior modification at home and at school to decrease external stimuli (e.g., by providing a quiet room without a lot of distractions), set consistent limits, and provide positive reinforcement.<sup>19</sup> Beneficial effects have been produced with clinical behavior therapy on a short-term basis, although the impact diminishes after the intervention stops and the long-term effects have not been studied.<sup>44</sup> Cognitive-behavioral treatment—which involves self-monitoring, verbal self-instruction, problem-solving strategies, and self-reinforcement—has not been shown to produce benefits in children with ADHD.<sup>14</sup>

## Alternative Therapies

Other treatments that have been used to treat ADHD include dietary management (exclusion of certain dietary components or food additives, nutritional supplementation), vitamin and mineral regimens, herbal and homeopathic remedies, biofeedback (e.g., use of electroencephalogram feedback to improve visual attention), hypnotherapy, meditation, and perceptual stimulation (e.g., listening to music to improve focus and attention).<sup>11,14</sup> Controlled studies of these therapies are lacking. The use of alternative therapies is not recommended as a substitute for standard therapies for ADHD.

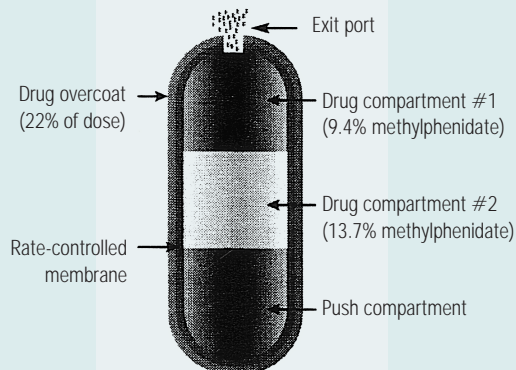
# Concerta™ (extended-release methylphenidate HCl)

Methylphenidate HCl has been available as immediate-release tablets (Ritalin) with a rapid onset and short duration (3 to 6 hours) of action.<sup>23</sup> It also has been available as sustained-release tablets (Ritalin-SR) with the drug embedded in a wax matrix and a slower onset and longer duration (about 8 hours) of action.<sup>23,27,45</sup> Concerta is a new extended-release tablet formulation of methylphenidate HCl that employs OROS osmotic technology—used in extended-release formulations of glipizide (Glucotrol XL), nifedipine (Procardia XL), and other drugs—to provide rate-controlled delivery of medication.<sup>25</sup> Concerta is designed to have a 12-hour duration of effect.<sup>25</sup> Peak plasma methylphenidate concentrations are achieved about 6 to 8 hours after administration of Concerta and are followed by a gradual decrease in plasma concentrations.<sup>25,46,47</sup> This results in a prolonged duration of action after once-daily morning dosing.

The capsule-shaped Concerta tablet has a drug overcoat containing 22% of the dose for immediate release after oral administration and a system core that contains the rest of the dose (Figure 1). The system core has a “push compartment” containing osmotic agents at one end of the tablet, two drug compartments, and a laser-drilled hole at the other end of the tablet. The core is coated with a semipermeable “rate-controlled” membrane. When gastrointestinal (GI) fluids pass through the semipermeable membrane into the system core, the osmotic agents in the push compartment expand, forcing the drug through the laser-drilled hole. By controlling the rate of fluid absorption into the system core, the semipermeable membrane controls the rate of drug release from the tablet, thus minimizing the fluctuations between peak and trough plasma concentrations associated with immediate-release formulations.<sup>25</sup>

Figure 1.

## The OROS® System



The tablet, including the semipermeable membrane, remains intact as the drug is delivered in the GI tract.<sup>25</sup> The tablet shell is later eliminated in the feces along with insoluble core components.

## Approved Indication

Concerta is indicated for the treatment of ADHD in individuals at least 6 years of age.<sup>25</sup> It is an integral part of a total treatment program that typically includes other measures (e.g., psychological, educational, social). The safety and efficacy of the drug in children younger than 6 years of age have not been established.<sup>25</sup>

The effectiveness of long-term use (i.e., more than 4 weeks) of Concerta has not been systematically evaluated in controlled trials, although data about longer periods of use are available for other dosage forms of methylphenidate HCl.<sup>22,25</sup> Therefore, the prescriber who elects to use Concerta for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual (see Dosage and Administration section).

## Contraindications

Concerta is contraindicated in patients with marked anxiety, tension, and agitation, because the drug may aggravate these symptoms. The drug also is contraindicated in patients with glaucoma, motor tics, or a family history or diagnosis of Tourette's syndrome. Other contraindications to the use of Concerta include treatment with monoamine oxidase inhibitors within the past 14 days and known hypersensitivity to the drug or other components of the formulation.<sup>25</sup>

## Pharmacokinetics

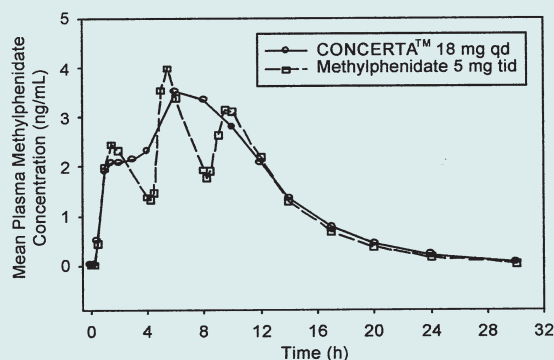
The pharmacokinetics of methylphenidate are similar in healthy adults and children with ADHD.<sup>27</sup> Most pharmacokinetic data about Concerta are derived from studies involving adults.

**Absorption.** Methylphenidate is absorbed readily in the GI tract.<sup>45</sup> After oral administration of Concerta to adults, plasma methylphenidate concentrations increase rapidly, reaching an initial maximum after about 1 or 2 hours.<sup>25,46</sup> This initial maximum is the result of dissolution of the drug overcoat. Concentrations increase gradually over the next several hours, reflecting slow release of the drug from the system core.<sup>25,46</sup>

The plasma concentration–time profile of methylphenidate given as a single 18-mg dose of Concerta was compared with that of three 5-mg immediate-release tablets given every 4 hours in an open-label, randomized, crossover study of 36 healthy adult volunteers.<sup>46</sup> Subjects receiving Concerta did not experience the fluctuations in plasma drug concentrations that occurred in subjects receiving immediate-release tablets (Figure 2).<sup>46</sup> The relative bioavailability of the two dosage forms was comparable.<sup>25,46</sup> The dose-normalized peak plasma concentration of methylphenidate was significantly lower for Concerta than for immediate-release methylphenidate.<sup>46</sup>

Figure 2.

## Mean Plasma Methylphenidate Concentrations With Concerta and Immediate-Release Methylphenidate<sup>a</sup>



<sup>a</sup>Mean plasma methylphenidate concentrations after a single 18-mg dose of Concerta and three doses of immediate-release methylphenidate 5 mg every 4 hours.

Source: Reference 25.

The area under the plasma concentration–time curve (AUC) and terminal half-life were similar after single and multiple doses of Concerta 18 mg in adults.<sup>47</sup> Clinically relevant accumulation of the drug does not occur with repeated administration. The variability in AUC was low, indicating that Concerta has predictable pharmacokinetics.<sup>47</sup>

Methylphenidate is a racemic mixture comprising *d*- and *l*-isomers. The *d*-isomer is more pharmacologically active than the *l*-isomer.<sup>45</sup> After administration of single 18-, 36-, and 54-mg doses of Concerta, the peak plasma concentration and AUC of the *d*-isomer of methylphenidate were proportional to dose.<sup>25</sup>

There were no differences in pharmacokinetics when Concerta was given with a high-fat breakfast, with a normal breakfast, or under fasting conditions to children 6 to 12 years of age.<sup>48</sup> There was no evidence of dose dumping in the presence or absence of food.<sup>25</sup>

**Distribution.** The plasma protein binding of methylphenidate is low (about 15%).<sup>27</sup> The drug penetrates the blood-brain barrier readily.<sup>27</sup>

**Metabolism and Elimination.** The metabolism of methylphenidate is stereospecific, resulting in substantially higher plasma concentrations of the more pharmacologically active *d*-isomer than the less active *l*-isomer.<sup>27</sup> In humans, methylphenidate is metabolized primarily by de-esterification to  $\alpha$ -phenyl-piperidine acetic acid (PPA), which has little or no pharmacologic activity.<sup>25</sup> In adults, the metabolism of Concerta (assessed as PPA levels) is similar to that of immediate-release methylphenidate tablets, regardless of whether single or multiple Concerta doses are used.<sup>25,47</sup>

Plasma methylphenidate concentrations decrease biexponentially (i.e., biphasically) after oral administration of Concerta to adults.<sup>25</sup> The half-life of methylphenidate was approximately 3.5 hours in adults receiving Concerta.<sup>46</sup>

After oral administration of radiolabeled methylphenidate in humans, about 90% of the radioactivity was recovered in the urine.<sup>25</sup> The main urinary metabolite was PPA, which accounted for approximately 80% of the dose (i.e., the renal route is not important for methylphenidate clearance).<sup>25</sup>

**Special Populations.** There is no experience with the use of Concerta in patients with renal insufficiency. Because the kidneys are not an important route for methylphenidate clearance, renal insufficiency is expected to have little effect on the pharmacokinetics of Concerta.<sup>25</sup> There is no experience with Concerta in patients with hepatic insufficiency.

## Dosage and Administration

Concerta is taken once daily in the morning, with or without food.<sup>25</sup> It should be swallowed whole with fluids and should not be chewed, divided, or crushed.

The recommended starting dosage for patients who have not been taking methylphenidate or who have been receiving other stimulants is 18 mg once daily. The daily dosage may be increased in 18-mg increments at approximately weekly intervals to a maximum of 54 mg/day as a single daily dose.<sup>25</sup>

The recommended dosage of Concerta for patients who have been taking immediate- or sustained-release methylphenidate 10 to 60 mg/day is listed in Table 3.<sup>25</sup> Clinical judgment should be used when selecting a starting dosage for patients who have been receiving other methylphenidate dosage regimens. The daily dosage may be increased in 18-mg increments at approximately weekly intervals to a maximum of 54 mg/day as a single daily dose.

Treatment with Concerta should be discontinued if no improvement is observed after appropriate dosage adjustment over a 1-month period. If paradoxical aggravation of symptoms or other adverse effects occur, the Concerta dosage should be reduced or, if necessary, the drug should be discontinued.

There is no body of evidence from controlled trials to indicate how long patients with ADHD should be treated with Concerta. It is generally agreed that pharmacologic treatment of the disorder may be needed for extended periods. When Concerta is used for extended periods, the drug should be discontinued periodically to assess the patient's function in the absence of the medication.

## Efficacy

The efficacy of Concerta in treating ADHD was demonstrated in three double-blind studies involving a total of 416 children 6 to 12 years of age who met the criteria for ADHD as listed in Table 1.<sup>25,49,50</sup> Concerta 18, 36, or 54 mg/day (as a single daily dose) was

Table 3.

## Recommended Concerta Starting Dosage in Patients Previously Treated With Methylphenidate Immediate- or Sustained-Release Tablets<sup>a</sup>

Previous Methylphenidate Dosage		Recommended Concerta Starting Dosage
Immediate-Release Tablets	Sustained-Release Tablets	
5 mg two or three times daily	20 mg/day	18 mg once daily in the morning
10 mg two or three times daily	40 mg/day	36 mg once daily in the morning
15 mg two or three times daily	60 mg/day	54 mg once daily in the morning <sup>b</sup>

<sup>a</sup>A change to Concerta is appropriate for patients who stand to benefit from once-daily administration, an onset of action within 1 to 2 hours after administration, and a duration of action of 12 hours. Clinical judgment should be used when selecting a starting dosage for patients who have been receiving methylphenidate dosage regimens other than those listed in this table. Concerta therapy may be initiated in newly diagnosed children at least 6 years of age using a dosage of 18 mg once daily for 1 week, with careful monitoring of response and adverse effects. The daily dosage may be increased in 18-mg increments at approximately weekly intervals, not to exceed 54 mg/day.

<sup>b</sup>Daily dosages exceeding 54 mg are not recommended.

Source: Reference 25.

compared with immediate-release methylphenidate 15, 30, or 45 mg/day (in three divided doses every 4 hours) or placebo in two 3-week, single-center, crossover studies and one 4-week, multicenter, parallel-group study.<sup>50</sup> Symptoms of inattention and overactivity were evaluated by community school teachers using the Inattention/Overactivity with Aggression (IOWA) Conners scale.<sup>51,52</sup> This scale is used widely by parents and teachers and consists of 10 behavioral items (five from the inattention/overactivity spectrum and five from the oppositional defiant disorder spectrum) scored on a 4-point scale.<sup>51</sup> Compared with placebo, Concerta consistently produced significant reductions in inattention and overactivity in all three controlled studies.<sup>25</sup> Comparable effects were observed with Concerta and immediate-release methylphenidate.<sup>49,50</sup> In an open-label study, IOWA Conners ratings similar to those observed with the active treatment groups in the three controlled clinical studies were maintained for up to 12 months in patients treated with Concerta (18, 36, and 54 mg once daily).<sup>53</sup>

In one of the 3-week controlled studies, inattention and behavior were evaluated in a structured laboratory school setting by specially trained teachers using the SKAMP laboratory school rating scale.<sup>49</sup> The SKAMP scale is a system for rating classroom manifestations of ADHD and the onset and duration of medication effects using 12 target behaviors scored on a 4-point scale.<sup>54</sup> The laboratory classroom was a naturalistic setting in which the children completed academic tasks throughout the day and also participated in recreational activities (e.g., recess periods, board games, free play). Concerta produced significant improvement in attention and behavior compared with placebo.<sup>49</sup> Efficacy was maintained through 12 hours after administration of a morning dose, and the beneficial effects of Concerta were sustained throughout the laboratory class-

room day. The onset of action was similar with Concerta and immediate-release methylphenidate.<sup>49</sup>

### Adverse Events

The safety of Concerta 18, 36, and 54 mg/day was evaluated in clinical trials of 755 subjects, including 469 children 6 to 13 years of age with ADHD and 286 healthy adult subjects.<sup>25</sup> Concerta generally was well tolerated. In a 4-week, placebo-controlled clinical study (see Efficacy section), the treatment-emergent adverse effects (regardless of causality) that occurred in 1% or more of patients and occurred more frequently among patients treated with Concerta than those receiving placebo were headache (14% with Concerta vs 10% with placebo), upper respiratory tract infection (8% vs 5%), abdominal pain/stomachache (7% vs 1%), anorexia (4% vs 0%), insomnia (4% vs 1%), increased cough (4% vs 2%), vomiting (4% vs 3%), pharyngitis (4% vs 3%), sinusitis (3% vs 0%), and dizziness (2% vs 0%).<sup>25</sup>

In uncontrolled studies lasting up to 12 months, 29 (6.6%) of 441 patients discontinued the study because of adverse events. The most common events resulting in discontinuation of Concerta were tics (1.8%), anorexia (0.9%), aggravation reaction (0.7%), hostility (0.7%), insomnia (0.7%), and somnolence (0.5%).<sup>25</sup> In the open-label study lasting up to 12 months (see Efficacy section), the cumulative incidence of new onset of tics was 8% after 10 months of treatment with Concerta.<sup>53</sup>

### Cautions

Concerta, like other methylphenidate products, is a schedule II controlled substance. It should be given cautiously to patients with a history of drug dependence or alcoholism. Chronic abuse can lead to marked tolerance and psychological dependence with varying

degrees of abnormal behavior.<sup>25</sup> Frank psychotic episodes can occur, especially with parenteral abuse.<sup>23,25</sup> Careful supervision is required during withdrawal after abuse because severe depression may occur.<sup>23,25</sup> Withdrawal after chronic therapeutic use may unmask symptoms of the underlying disorder that require follow-up.

Sufficient data on the safety of long-term use of methylphenidate in children are not yet available. Periodic complete blood counts with differential and platelet counts are recommended during prolonged therapy.<sup>25</sup>

Although a causal relationship has not been established, suppression of growth (i.e., weight gain, height increase, or both) has been reported with long-term use of stimulants in children.<sup>25</sup> Therefore, patients requiring long-term Concerta therapy should be monitored carefully. Treatment should be interrupted in patients who are not growing or gaining weight as expected.

Concerta should not be used to treat severe depression or to prevent or treat normal fatigue states.<sup>25</sup>

Clinical experience suggests that in psychotic patients, administration of methylphenidate may exacerbate symptoms of behavior disturbance and thought disorder.<sup>25</sup>

There is evidence that methylphenidate may lower the convulsive threshold in patients with a history of seizures, patients with a history of electroencephalogram abnormalities in the absence of seizures, or very rarely, patients without a history of seizures or electroencephalogram abnormalities.<sup>23</sup> Concerta therapy should be discontinued if seizures occur.<sup>25</sup>

Because Concerta tablets are nondeformable and do not change shape appreciably in the GI tract, the drug ordinarily should not be administered to patients with preexisting severe pathologic or iatrogenic GI narrowing (e.g., small bowel inflammatory disease; “short gut” syndrome due to adhesions or decreased transit time; history of peritonitis, cystic fibrosis, chronic intestinal pseudo-obstruction, or Meckel’s diverticulum).<sup>25</sup> Rare reports of obstructive symptoms in patients with known strictures have been associated with ingestion of other drugs in nondeformable controlled-release formulations. Concerta should be used only in patients who are able to swallow the tablets whole because the controlled-release characteristics of the product require that the tablets remain intact.

Concerta should be used with caution in patients with hypertension.<sup>25</sup> Blood pressure should be monitored at appropriate intervals in patients receiving Concerta, especially patients with hypertension.<sup>25</sup> In the 3-week controlled clinical studies (see Efficacy section), both Concerta and immediate-release methylphenidate increased daytime resting pulse by an average of 2 to 6 beats per minute and systolic and diastolic blood pressure by roughly 1 to 4 mm Hg compared with placebo.<sup>25</sup>

Methylphenidate may cause blurred vision and difficulty with accommodation of the eye.<sup>25</sup> Symptoms of visual disturbances have been encountered in rare cases.

Concerta is classified in FDA pregnancy category C.<sup>25</sup> Methylphenidate has been shown to have teratogenic effects in animals given the equivalent of approximately 100 times the maximum recommended human dose on the basis of body weight. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Concerta should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.<sup>25</sup>

It is not known whether methylphenidate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised if Concerta is administered to a woman who is breast-feeding.<sup>25</sup>

## Drug Interactions

Use of Concerta with or within 14 days after discontinuing monoamine oxidase inhibitors is contraindicated because of the risk of hypertensive crisis.<sup>25</sup> Concerta should be used cautiously with pressor agents (e.g., phenylpropanolamine and other sympathomimetic amines) because of the risk of additive blood pressure increases.<sup>23,25</sup>

Human pharmacology studies have shown that methylphenidate may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (e.g., phenobarbital, phenytoin, primidone), and certain antidepressants (tricyclic antidepressants and selective serotonin reuptake inhibitors).<sup>23,25</sup> The dosage of these drugs may need to be decreased when they are given concomitantly with methylphenidate. Methylphenidate may antagonize the blood pressure-lowering effect of bretylium and guanethidine.<sup>23</sup>

Serious adverse effects have been reported with concomitant use of methylphenidate and clonidine (see Clonidine and Guanfacine section), although a causal relationship has not been established.<sup>25</sup> The safety of using methylphenidate in combination with clonidine or other centrally acting  $\alpha_2$ -adrenergic agonists has not been evaluated systematically.

## Safety in Overdose Situations

Signs and symptoms of acute methylphenidate overdose result primarily from overstimulation of the CNS and excessive sympathomimetic effects and may include vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions (sometimes followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, mydriasis, and dryness of mucous membranes.<sup>23,25</sup> Treatment consists of appropriate supportive measures. The patient should be protected against self-injury and external stimuli that could aggravate the excessive stimulation already present.<sup>25</sup> Gastric contents may be evacuated by gastric lavage as indicated. Agitation and seizures should be controlled and the airway should be protected before performing gastric lavage. Other measures to

detoxify the gut include administration of activated charcoal and a cathartic. Intensive care should be provided to maintain adequate circulation and respiratory exchange. External cooling procedures may be required for hyperpyrexia.<sup>25</sup>

The efficacy of peritoneal dialysis and extracorporeal hemodialysis for treating Concerta overdose has not been established. The prolonged release of methylphenidate from Concerta should be considered in overdose situations.

Clinicians may wish to contact a certified poison control center for up-to-date guidance and advice about treating methylphenidate overdoses. The possibility of multiple drug ingestion should be considered.

## How Supplied

Concerta is available as yellow 18-mg tablets; white 36-mg tablets; and brownish-red, 54-mg tablets.

## Pharmaceutical Care Considerations

Pharmacists are readily accessible sources of information about drug therapy for ADHD. Parents and caregivers of children with the disorder may seek the pharmacist's advice about the safety and efficacy of medications and alternative therapies. Some parents are reluctant to use medication for their child because of concerns about adverse effects, long-term safety, addiction, and the social stigma of using medication to treat the disorder in a child.<sup>55</sup> The pharmacist can place in perspective what is known about the safety, efficacy, and abuse potential of various therapies. Pharmacists also can dispel myths and correct misperceptions about the cause and treatment of the disorder.<sup>56</sup> For example, the pharmacist might explain that ADHD is a medical condition—not the result of poor parenting, laziness, or excessive sugar consumption—and that stimulants increase levels

## Concerta™ at a Glance

<b>What It Is:</b>	Methylphenidate HCl, a central nervous system stimulant
<b>How It Works:</b>	May increase neurotransmitter (dopamine and norepinephrine) levels in areas of the brain that regulate attention, motor function, and behavior
<b>What It Does:</b>	Improves attention and behavior and reduces hyperactivity
<b>Indication:</b>	Treatment of attention deficit hyperactivity disorder in adults and children at least 6 years of age
<b>How Supplied:</b>	Yellow 18-mg, white 36-mg, and brownish-red 54-mg extended-release tablets using OROS osmotic technology
<b>Dosage:</b>	18 mg to 54 mg once daily in the morning, with or without food
<b>Most Common Adverse Events:</b>	Headache, upper respiratory tract infection, abdominal pain, anorexia, insomnia, increased cough, vomiting, pharyngitis, sinusitis, dizziness
<b>Contraindications:</b>	Marked anxiety, tension, and agitation; glaucoma; motor tics or a family history or diagnosis of Tourette's syndrome; treatment with monoamine oxidase inhibitors within the past 14 days; known hypersensitivity to the drug or other components of the formulation
<b>Drug Interactions:</b>	Anticonvulsants (e.g., phenobarbital, phenytoin, primidone), coumarin anticoagulants, monoamine oxidase inhibitors, pressor agents, selective serotonin reuptake inhibitors, tricyclic antidepressants
<b>Use in Pregnancy:</b>	Use only if the potential benefit justifies the potential risk to the fetus

of neurotransmitters in brain areas that regulate attention, activity, and behavior.

Pharmaceutical care should be provided for patients receiving drug therapy for ADHD to optimize patient outcomes. A complete patient history, including medications (particularly response to drug therapies used for ADHD) and herbal remedies, should be obtained. The pharmacist should devise a pharmaceutical care plan that addresses all aspects of drug therapy and anticipates problems to prevent or minimize them. At each follow-up visit, the pharmacist should ask about response to therapy (degree and duration of symptom control), adverse effects, and other problems with drug therapy. Failure to control symptoms adequately could be the result of patient nonadherence, misdiagnosis, or comorbidity. The pharmacist should identify barriers to adherence and develop strategies to overcome them to the extent possible. Patients in whom misdiagnosis or undiagnosed comorbidity is suspected should be referred to an appropriate health care professional. Patients, parents, and caregivers should be warned not to discontinue drug therapy abruptly unless directed to do so by the prescriber. If stimulant drug therapy is used for long periods, annual complete blood counts should be encouraged.

The extended duration of action offered by Concerta may help to solve a number of drug therapy problems among patients with ADHD. For example, the need for multiple daily doses of a short-acting preparation may pose a problem at school or in the workplace. Concerta may be a good alternative for children who attend schools where it is disruptive or otherwise problematic to arrange for the child to receive a dose at school (e.g., because of local regulations restricting school personnel from administering psychoactive medication to students). Once-daily administration in the privacy of the home avoids the social stigma and overcomes concerns about diversion of controlled substances in the school or work setting. Also, the effect of short-acting medication may wear off in the afternoon; once-daily administration of an extended-release formulation may be particularly helpful for children who need a longer duration of symptom control (e.g., for after-school activities).

## Summary

Attention deficit hyperactivity disorder can have a tremendous impact on emotional health, social relationships, and academic and vocational success. Although the pathogenesis remains to be clarified, it appears to involve genetic and neurobiologic abnormalities involving catecholamine neurotransmitters in the CNS. Drug therapy is more effective than psychosocial therapy for ADHD, and stimulants are regarded as the most effective medications. Their mechanism of action in treating the disorder is unclear but may involve increases in neurotransmitter levels in the CNS.

Concerta is a new formulation of methylphenidate HCl that improves inattention, motor function, and behavior to the same

extent as immediate-release tablets but has a longer duration of effect. This prolonged action permits once-daily administration and helps to avoid problems with the fluctuations in plasma concentration seen with immediate-release tablets. Concerta generally is well tolerated. The long-term safety of Concerta and other stimulants used to treat ADHD remains to be clarified.

Pharmacists can provide parents, caregivers, and patients with information about the efficacy of medications and other therapies for ADHD. In monitoring response to therapy, the pharmacist can identify strategies to improve patient adherence and drug tolerability as well as determine whether therapeutic goals are being achieved.

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## What You Need to Know About Attention Deficit Hyperactivity Disorder and Concerta™

### 1. My child has attention deficit hyperactivity disorder. What causes it?

Attention deficit hyperactivity disorder (ADHD) is a group of symptoms—inattention (for example, not listening or being readily distracted) or hyperactivity and impulsivity (for example, running around a lot or restlessness). No one knows exactly what causes ADHD; it probably is the result of a combination of factors. Attention deficit hyperactivity disorder tends to run in families, which suggests that it may be the result of an inherited abnormality in the genes. Attention deficit hyperactivity disorder is not the result of poor parenting, laziness, or eating too much sugar or food additives.

Some children outgrow ADHD in their teen years. Others have symptoms into adulthood, although the symptoms usually change over time. For example, hyperactivity tends to decrease over time, although inattention often does not improve.

### 2. The doctor prescribed Concerta. What is it and how does it work?

Concerta is a stimulant medication similar to Ritalin, a medication that many children and adults take for ADHD. Concerta starts to work faster and goes on working longer than Ritalin. Many people must take Ritalin several times a day to make sure that its effect does not wear off. Because Concerta is designed to work for 12 hours, it is not necessary to take extra doses during the day.

Concerta improves the symptoms of ADHD (inattention, hyperactivity) and behavior. Scientists are not sure exactly how Concerta works in people with ADHD. It is thought to increase the amounts of certain natural chemicals in areas of the brain that control attention, activity, and behavior. Concerta must be taken every day to be effective.

### 3. How and when should Concerta be taken?

Concerta usually is taken once daily in the morning. Follow the instructions on the prescription label, and ask your pharmacist or health care provider if you have any questions.

Concerta may be taken with or without food. The tablets should be swallowed whole with water, milk, juice, or another beverage. Do not divide or crush Concerta tablets or allow your child to chew them.

Keep all appointments with the health care provider. It may be necessary to adjust the dosage of Concerta. However, do not adjust the dosage on your own.

### 4. What side effects might be expected from Concerta?

Possible side effects from Concerta include headache, stomachache, sleeplessness, and decreased appetite. Contact your health care provider if these effects are severe or persist.

Because of the way the Concerta tablet is designed, it does not dissolve completely. The empty tablet shell passes through the body after all of the medication is released. So, do not be alarmed if you see something that looks like a tablet in the stool. This is normal.

### 5. Is it safe to take Concerta with other medications?

Some combinations of medications can cause problems. Tell every pharmacist and health care provider that you go to about all the prescription and nonprescription medications and herbal remedies that your child takes, especially other medication for ADHD, antidepressants, medication for high blood pressure, blood thinners, and seizure medications. Write the names on a piece of paper, or if you prefer, bring the containers with you when you visit the pharmacy and health care provider's office.

### 6. Where can I find additional information about Concerta?

Ask your pharmacist or health care provider, call 1-888-440-7903, or go to <http://www.concerta.net> on the World Wide Web.





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