

Guanfacine (Intuniv) for Attention-Deficit/Hyperactivity Disorder

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STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

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Guanfacine (Intuniv) is an extended-release, non-central nervous system stimulant approved for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children six to 17 years of age; however, it appears to be most effective in children 12 years or younger. Similar to clonidine (Catapres), it works as a selective agonist for the α_{2A} -adrenergic receptor, although the actual mechanism of action is not known.

| Drug | Starting dosage | Dose form | Approximate monthly cost* |
|----------------------|-----------------|--|---------------------------|
| Guanfacine (Intuniv) | 1 mg per day | 1-mg, 2-mg, 3-mg, or 4-mg extended-release tablets | \$156 (2 to 3 mg per day) |

*—Estimated retail price of one month's treatment based on information obtained at <http://www.drugstore.com> (accessed August 16, 2010).

SAFETY

Guanfacine can cause hypotension, although it does not cause symptoms in most patients, and changes in blood pressure are usually small. Approximately 1 percent of children taking guanfacine will experience orthostatic hypotension. Syncope also occurs in about 1 percent of children, but it is not clear whether this is related to the drop in blood pressure or is a separate adverse effect. Changes on electrocardiography, including bradycardia, are rare but have occurred in clinical trials. Abrupt withdrawal of guanfacine should be avoided to decrease the risk of notable changes in blood pressure. Guanfacine is U.S. Food and Drug Administration pregnancy category B.¹

TOLERABILITY

Sedation is common with guanfacine treatment and can be severe in a small number of children. Somnolence and fatigue are also common, affecting 9 to 40 percent of children.^{2,3} These effects generally occur within two to three weeks of starting therapy and

tend to decrease over time; most patients report not having these effects by the end of the eight- to nine-week treatment period.²⁻⁴ The dosage should be slowly titrated up to avoid these adverse effects. In clinical trials, 12 percent of patients taking guanfacine discontinued therapy, compared with 4 percent of those taking placebo. The most common reasons for discontinuation were somnolence and sedation.¹ Patients on long-term (i.e., 12 to 24 months) guanfacine therapy reported adverse effects similar to those seen in short-term studies, with somnolence, sedation, and fatigue being the most common. As with short-term therapy, the adverse effects from long-term therapy generally decrease over time.²⁻⁶

EFFECTIVENESS

Guanfacine is effective in the short-term (i.e., eight to nine weeks) treatment of ADHD. Dosages of 1 to 4 mg per day decrease scores on the ADHD Rating Scale-IV by an average of 17 to 21 points, compared with a decrease of 9 to 12 points with placebo.^{2,3} ►

When adjusted for age, the changes in ADHD Rating Scale-IV scores were not statistically significant compared with the placebo group in patients 13 to 17 years of age, but were for patients six to 12 years of age.^{2,3} Therefore, effectiveness in children 13 to 17 years of age is questionable. Both physician ratings and parent assessments expressed marked improvement in more children receiving guanfacine compared with those receiving placebo. About twice as many children receiving guanfacine had statistically significant improvement on the Clinical Global Impressions Improvement scale. Similarly, 36 to 62 percent of patients taking guanfacine had statistically significant improvement on the Parent Global Assessment scale compared with 30 percent of those taking placebo.²

The duration of action of guanfacine, at least at lower dosages, is no more than eight hours, and higher dosages may be needed to produce sustained effectiveness.^{2,3} Guanfacine has not been compared directly with other ADHD medications, including psychostimulant medications, clonidine, and atomoxetine (Strattera).

PRICE

Guanfacine (2 to 3 mg per day) costs approximately \$156 per month. Atomoxetine, the other noncontrolled substance used to treat ADHD, is similarly priced at approximately \$203 per month for a dosage of 80 mg per day. A typical stimulant medication, methylphenidate extended-release (Ritalin SR; 20 mg per day), costs approximately \$86 per month.

SIMPLICITY

The starting dosage of guanfacine is 1 mg per day. The dosage can be titrated up in increments of 1 mg per week to a maximum dosage of 4 mg per day. Tablets should not be chewed or crushed. Guanfacine should be given on a daily basis for the entire week, not just on school days, to avoid issues

with returning or worsening somnolence and potential, but rare, increases in blood pressure. Patients who miss two or more consecutive doses may need to restart therapy at 1 mg per day and then titrate the dosage up based on patient tolerability. To discontinue guanfacine, the dosage should be tapered by 1 mg every three to seven days.¹

Bottom Line

Guanfacine is an effective short-term treatment option for ADHD in children six to 12 years of age. Sedation is a marked problem in many children. Patients should take the medication daily to avoid adverse effects that occur with abrupt discontinuation or when the guanfacine is restarted.

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REFERENCES

1. Intuniv (guanfacine) extended-release tablets [product information]. Wayne, Pa.: Shire Pharmaceuticals; 2009. http://www.intuniv.com/documents/INTUNIV_Full_Prescribing_Information.pdf. Accessed March 3, 2010.
2. Sallee FR, McGough J, Wigal T, Donahue J, Lyne A, Biederman J; SPD503 Study Group. Guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder: a placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2009;48(2):155-165.
3. Biederman J, Melmed RD, Patel A, et al.; SPD503 Study Group. A randomized, double-blind, placebo-controlled study of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder. *Pediatrics*. 2008;121(1):e73-84.
4. Faraone SV, Glatt SJ. Effects of extended-release guanfacine on ADHD symptoms and sedation-related adverse events in children with ADHD. *J Atten Disord*. 2010;13(5):532-538.
5. Biederman J, Melmed RD, Patel A, McBurnett K, Donahue J, Lyne A. Long-term, open-label extension study of guanfacine extended release in children and adolescents with ADHD. *CNS Spectr*. 2008;13(12):1047-1055.
6. Sallee FR, Lyne A, Wigal T, McGough JJ. Long-term safety and efficacy of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2009;19(3):215-226. ■