The U.S. Food and Drug Administration (FDA) has approved risperidone (Risperdal®), olanzapine (Zyprexa®), quetiapine (Seroquel®), ziprasidone (Geodon®), and aripiprazole (Abilify®) for the treatment of schizophrenia and bipolar mania in adults, whereas clozapine (Clozaril®) is approved for treatment-resistant schizophrenia and to reduce the risk of recurrent suicidal behaviors in schizophrenia. None of these atypical antipsychotic drugs are FDA approved for any indication in children and adolescents. However, they are increasingly being used for various disorders seen in younger patients (DelBello & Grcevich, 2004) and are now more commonly prescribed than older-generation (typical) antipsychotic agents in pediatric patients (Findling & McNamara, 2004).

In particular, the atypical antipsychotic drugs are used relatively more often in pediatric patients for the behavioral problems associated with pervasive developmental disorders, mental retardation, and conduct disorders. The primary rationale for using these unapproved drugs in younger patients is the high prevalence and associated...
disability of these and other early-onset mental disorders that might respond to antipsychotic therapy (McConville & Sorter, 2004). In addition, their relative efficacy, tolerability, and safety (compared to typical antipsychotic agents) in adults have been cited to support their use in children and adolescents. Finally, anecdotal reports, case series, retrospective chart reviews, open-label studies, and randomized, controlled studies that provide further justification for their pediatric use have been published. The use of atypical antipsychotic drug therapies for children and adolescents is described in this article.

**CLOzapine (Clozaril)**

Clozapine was the first atypical antipsychotic agent approved for use in the United States. Since 1992, various published reports have suggested that clozapine is effective for pediatric patients (age 6 and older) with treatment-resistant schizophrenia, bipolar disorder, aggression, and tardive dyskinesia (Cheng-Shannon, McGough, Pataki, & McCracken, 2004). The only randomized, double-blind, controlled study found that clozapine was superior to haloperidol in childhood-onset, treatment-resistant schizophrenia (Kumra et al., 1996).

Typical starting dosage for pediatric patients is 6.25 to 12.5 mg per day (therapeutic range is 50 to 600 mg per day). Common side effects are sedation, increased salivation, weight gain, tachycardia, and orthostatic hypotension (Findling & McNamara, 2004). Rare adverse effects include hyperglycemia, hyperlipidemia, increased liver enzymes, seizures, and agranulocytosis, which requires weekly or biweekly monitoring of white blood cell counts.

Compared to all other antipsychotic drugs, clozapine is less likely to be associated with Parkinsonian side effects (i.e., tremors, muscle rigidity, bradykinesia, akathisia), hyperprolactinemia, tardive dyskinesia, or neuroleptic malignant syndrome. However, clozapine is considered a treatment of last resort because of the risk of serious side effects and the need for frequent blood monitoring.

**Risperidone (Risperdal)**

Among the atypical antipsychotic agents, risperidone is the best studied in pediatric patients (age 2 and older), although it has not been rigorously investigated in those with schizophrenia or bipolar disorder. Numerous reports published since 1994 have suggested that it is effective for childhood-onset schizophrenia, bipolar disorder, tic disorders, and behavioral problems associated with pervasive developmental disorders, mental retardation, and conduct disorders (Cheng-Shannon et al., 2004). A single randomized, double-blind, controlled study found that risperidone and olanzapine were slightly more effective than haloperidol for psychotic symptoms in a group of young patients with mixed diagnoses (i.e., schizophrenia and psychotic mood disorders) (Sikich, Hamer, Bashford, Sheitman, & Lieberman, 2004). No controlled studies have been conducted to date with risperidone for nonpsychotic bipolar disorder. Several randomized, double-blind, controlled studies (using active controls and/or placebo controls) have found risperidone to be effective for the tics associated with Tourette’s syndrome (Dion, Annable, Sandor, & Chouinard, 2002; Gaffney et al., 2002) and for the behavioral problems associated with pervasive developmental disorders, mental retardation, and conduct disorders, such as hyperactivity, aggression, agitation, and self-harm (Findling, Aman, Eerdekens, Derivan, & Lyons, 2004; McDougle et al., 2005).

Typical starting dosage is 0.25 to 0.5 mg per day (therapeutic range is 1 to 6 mg per day). Common side effects are sedation and weight gain (Findling & McNamara, 2004), and a rare adverse effect is increased liver enzymes. Compared to other atypical antipsychotic drugs, risperidone is somewhat more likely to be associated with Parkinsonian side effects and hyperprolactinemia, es-

None of these atypical antipsychotic drugs are FDA approved for any indication in children and adolescents. However, they are increasingly being used for various disorders seen in younger patients.
especially with higher dosages. Clinical monitoring for tardive dyskinesia and neuroleptic malignant syndrome is warranted, although these adverse effects are less likely to occur than with typical antipsychotic agents. With careful clinical monitoring, risperidone can be safely and effectively used in combination with other psychotropic drugs.

OLANZAPINE (ZYPREXA)

Compared to risperidone, olanzapine has not been well studied in pediatric patients. Since 1997, various published reports have described its use in young patients (age 5 and older) with childhood-onset schizophrenia, bipolar disorder, tic disorders, eating disorders, and behavioral problems associated with pervasive developmental disorders and mental retardation (Cheng-Shannon et al., 2004). As described above, one controlled study found that olanzapine and risperidone were slightly more effective than haloperidol for psychotic symptoms in patients with mixed diagnoses (Sikich et al., 2004). No other controlled studies have been reported to date with olanzapine in pediatric patients.

Typical starting dosage is 2.5 to 5 mg per day (therapeutic range is 2.5 to 20 mg per day). The side effects of sedation and weight gain may be more common with olanzapine than with other atypical antipsychotic agents, except clozapine (Findling & McNamara, 2004). Rare adverse effects are hyperglycemia, hyperlipidemia, and increased liver enzymes. Olanzapine is not usually associated with Parkinsonian side effects, hyperprolactinemia, tardive dyskinesia, or neuroleptic malignant syndrome, although clinical monitoring is prudent. Other reports published since 1998 have described its use in young patients (age 5 and older) with childhood-onset schizophrenia, bipolar disorder, tic disorders, and behavioral problems associated with pervasive developmental disorders (Cheng-Shannon et al., 2004).

Ziprasidone (Geodon)

There are relatively few reports in the literature about the use of ziprasidone in pediatric patients. The only randomized, double-blind, controlled study found that ziprasidone was superior to placebo for the tics associated with Tourette’s syndrome (Sallee et al., 2000). Since 2000, a few published reports have described its use in young patients (age 7 and older) with bipolar disorder, tic disorders, and behavioral problems associated with pervasive developmental disorders (Cheng-Shannon et al., 2004).

Typical starting dosage is 20 mg per day (therapeutic range is 20 to 160 mg per day). Side effects include sedation (Findling & McNamara, 2004). Rare adverse effects are cardiac electrocardiogram changes (i.e., prolongation of the QTC interval), but this occurs only at excessively high dosages or in the presence of other risk factors for QTC prolongation. Ziprasidone is not usually associated with weight gain, Parkinsonian side effects, hyperprolactinemia, tardive dyskinesia, or neuroleptic malignant syndrome, but clinical monitoring is recommended.

ARIPIPRAZOLE (ABILIFY)

Aripiprazole is the newest atypical antipsychotic agent. Open-label studies and retrospective chart reviews have described its use in pediatric patients (age 6 and older) with bipolar disorder (Barzman et al., 2002). Other reports published since 1998 have described its use in young patients (age 5 and older) with childhood-onset schizophrenia, bipolar disorder, tic disorders, and behavioral problems associated with pervasive developmental disorders (Cheng-Shannon et al., 2004).

Typical starting dosage is 25 to 50 mg per day (therapeutic range is 25 to 800 mg per day). Common side effects include sedation and weight gain (Findling & McNamara, 2004). Rare adverse effects are tachycardia and orthostatic hypotension. Aripiprazole is not usually associated with Parkinsonian side effects, hyperprolactinemia, tardive dyskinesia, or neuroleptic malignant syndrome, but patients should be monitored.


