

Approval Based on Two Trials

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and bipolar disorder indications down to age 10 years. The recommended dose for the new indication is 5- 10 mg day (starting at 2 mg per day, with the maximum dose of 15 mg per day).

The effectiveness of aripiprazole for the autistic disorder indication was established in two 8-week multicenter studies of children and adolescents aged 6-17 years (more than 75% were younger than age 13 years), according to the revised label. They met the DSM-IV criteria for autistic disorder and exhibited behaviors that included tantrums, aggression, and/or self-injurious behavior.

In one study of 98 children and adolescents, those on aripiprazole (at a starting dose of 2 mg/day increasing up to 15 mg per day based on clinical response), had significantly improved scores when compared to those on placebo at 8 weeks on two scales: the irritability subscale of the Aberrant Behavior Checklist (ABC-I), a caregiver-rated assessment tool, and the Clinical Global Impression-Improvement (CGI-I) scale, a tool used to monitor treatment outcomes in psychiatric disorders.

In the second study of 218 children and adolescents, those on a fixed dose of aripiprazole (5 mg, 10 mg, or 15 mg per day) had significantly improved scores on the ABC-I Subscale, compared with those on placebo.

In a pooled analysis of the two studies, mean weight gain among those on aripiprazole was 1.6 kg, compared with 0.4 kg among those on placebo. During the study, 26% of those on aripiprazole and 7% of those on placebo experienced clinically significant weight gain, defined as at least a 7% change from baseline, according to the company statement.

Other common adverse events that were more common among treated patients included sedation, affecting 21% of those on aripiprazole compared with 4% of those on placebo, fatigue (17% vs. 2%), vomiting (14% vs. 7%), somnolence (10% vs. 4%), tremor (10% vs. 0%), drooling (9% vs. 0%), and extrapyramidal disorder (6% vs. 0%).

These studies were "not designed or intended to evaluate" aripiprazole for treatment of the core symptoms of autistic disorder, the company statement said. ■

PERSPECTIVE: Treatment Option Is Welcome

It's nice to have a second option for treating irritability in children with autism. Irritability and aggression in children with autism are frequently what lead to disruption of placement in the school and home setting, and are often the reason these children are sent to the hospital or residential treatment facility. It's helpful for physicians who are treating developmentally disabled children to have two treatment options. Almost 300 children were studied and the amount of safety and efficacy data is reassuring to physicians who are considering prescribing this medicine.

Aripiprazole can make a huge difference in quality of life in these children. Children's National Medical Center was one of the sites for the fixed-dose study of 218 children and adolescents. We saw cases where an autistic child could sit through church services. We saw autistic children who were yelling, kicking, screaming, head banging, and having tantrums most of the day most days of the week, and who improved to the point where if, for example, they did not get something they wanted at the grocery store, they would have a temper tantrum that would last only a few minutes.

One mother said her child was able to sit through an hour-long awards ceremony for a sibling, which had never would have happened before. Another child in the study actually opened up a book and looked at the

pictures and letters—instead of ripping it apart and throwing it across the room.

The label lists the adverse effects associated with treatment. Sleepiness is one of the side effects that affect some children. Some parents of children in the study said their children slept better at night, which was probably a side effect of the medicine. There was more weight gain among those on treatment, compared with those on placebo, but we need to look at body mass index, because

most of the children in the studies were under 13 and were still growing. We also need to keep in mind that parents may use food as a reward when trying to calm down their autistic children and to change their behavior.

Aripiprazole is also available in a liquid formulation, which can be used for children who can't or won't swallow pills. Considering the large number of children with autism in the United States, it is helpful to have medicine that works for irritability, one of the big problems parents and schools have to confront.

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CMS Adds Geriatric Code

The Centers for Medicare and Medicaid Services has established a new physician specialty code for geriatric psychiatry. The code, 27, will go into effect April 1, 2010, the agency announced in late October. CMS directed all its contractors to recognize the new physician specialty code on all claims.

Dr. Nemeroff Lands in Miami

Dr. Charles B. Nemeroff, who was hounded by charges of conflicts of interest in his biological studies of neuropsychiatric disorders, has left Emory University, Atlanta, for the University of Miami. He will be professor and chairman of the department of psychiatry and behavioral sciences. While at Emory, Dr. Nemeroff was accused of failing to disclose \$800,000 in payments from GlaxoSmithKline while he was directing National Institutes of Health studies that used some of that company's products. Emory subsequently stripped him of his psychiatry chairmanship and blocked him from seeking NIH grants for 2 years. It also prompted Emory to revise its conflict rules. According to a statement from Miami's Miller School of Medicine, Dr. Nemeroff plans to work on mental health and aging, HIV, drug abuse, and links between depression and cancer and heart disease.

Shire Receives OIG Subpoena

The British-based pharmaceutical company Shire plc has received a subpoena from the Office of the Inspector General of the U.S. Department of Health and Human Services seeking documents related to the sales and marketing of Adderall XR (amphetamine/dextroamphetamine), Daytrana (methylphenidate), and Vyvanse (lisdexamfetamine). Shire disclosed the subpoena in a statement with its third-quarter 2009 earnings announcement, which said sales of Adderall XR dropped 74% in the quarter. But Vyvanse sales continued to grow, partly because of the Food and Drug Administration's rejection of a generic competitor earlier this year and partly because of a 10% growth in the market for attention-deficit/hyperactivity disorder treatments, Shire said. The company also said it is about to launch its latest drug for ADHD, Intuniv (guanfacine).

Huge Seroquel Settlement

AstraZeneca will pay \$520 million to settle several legal proceedings relating to its atypical antipsychotic Seroquel (quetiapine). The settlement was for two federal investigations and two whistleblower (qui tam) suits. In its third quarter- 2009 earnings filing, the company said that the qui tam suits were related to two investigations by the U.S. Attorney's Office in

Philadelphia. One concerns off-label sales and marketing, and the second is about "selected physicians who participated in clinical trials involving Seroquel," the company said. AstraZeneca reached an agreement in principle to resolve the investigations in September, which included the payout. Meanwhile, Seroquel sales continue to rise. Compared with those last year, sales increased 16% in the United States for the 9 months ending Sept. 30, 2009, totaling \$2.5 billion. Sales in the rest of the world increased 9%, to \$1 billion, despite a 73% decline in Canada because of the introduction of a generic.

Risperdal Litigation Grows

There are now 425 cases pending against Johnson & Johnson's Ortho-McNeil-Janssen Pharmaceuticals Inc. alleging various damages from the atypical antipsychotic Risperdal (risperidone). The figure was disclosed in the company's third-quarter earnings statement. The company also said attorneys general in eight states and the Office of General Counsel of Pennsylvania are seeking reimbursement for public funds spent on off-label prescriptions and to treat adverse reactions. The Texas attorney general has joined a whistleblower suit seeking similar relief. More may be coming: Attorneys general in 40 other states have taken an interest in such litigation and have secured a ruling that stays the statute of limitations while they investigate. Six union health plans also have sued to recover alleged overpayments and have sought certification for a class action. Meanwhile, Risperdal sales dropped 60% in the first 9 months of 2009, partly because of generic competitors. But those sales are being replaced by the company's Risperdal Consta, which had revenues of \$1 billion from January to October.

More Autism Grants From AARA

The NIH has awarded 50 grants for autism research totaling \$65 million. The funds were provided by the American Recovery and Reinvestment Act (ARRA), known popularly as the economic stimulus package. A statement from the National Institute of Mental Health said all the grants were awarded based on how well they met short-term research objectives outlined in a plan devised by Interagency Autism Coordinating Committee. Much of the data from the studies will be available to other researchers through the National Database for Autism Research. NIMH's director, Dr. Thomas R. Insel, said the studies "hold the best promise of revealing what causes autism, how it might be prevented, what treatments are effective, and how service needs change across the lifespan."

—Alicia Ault