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NEWS

Newer Atypical Antipsychotics Draw Praise

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EXPERT ANALYSIS FROM A PSYCHOPHARMACOLOGY CONFERENCE SPONSORED BY THE UNIVERSITY OF ARIZONA

TUCSON, ARIZ. – The most noteworthy characteristic of lurasidone, the newest antipsychotic agent to reach the market, is its exceptionally favorable metabolic profile, according to Dr. Henry A. Nasrallah.

"It has placebo-level metabolic effects," said Dr. Nasrallah, professor of psychiatry and neuroscience at the University of Cincinnati. "The metabolic profile is better than for Geodon [ziprasidone] or Abilify [aripiprazole], which are currently accepted as the least metabolically adverse atypical antipsychotics."

Dr. Henry A. Nasrallah

Lurasidone (Latuda) is an oral atypical antipsychotic approved earlier this year for the treatment of schizophrenia and is just now reaching pharmacy shelves. Long-term studies indicate that the drug is weight neutral, with no weight gain over baseline even after 6 and 12 months of treatment. Indeed, in a 12-month head-to-head comparative study, the lurasidone-treated group actually lost a mean of 0.9 kg, while those on risperidone (Risperdal) gained an average of 2.6 kg. Lurasidone's long-term impact on lipids and blood glucose has been similarly benign.

Also, intriguing preliminary evidence suggests that lurasidone might have antidepressant and cognitive enhancement effects, according to the psychiatrist. The dose is 40-80 mg once daily.

Last year saw marketing approval for asenapine (Saphris), the first sublingual antipsychotic agent. Asenapine is mucosally absorbed, so it goes directly into the bloodstream without first passing through the stomach and liver. That means fewer drug-drug interactions. It also makes asenapine a safer choice for patients prone to overdose; mucosal absorption renders fatal overdose extremely difficult, Dr. Nasrallah said at a psychopharmacology conference sponsored by the University of Arizona.

The dosing of asenapine is 5 mg b.i.d. Weight gain is relatively modest, compared with that associated with many of the atypical antipsychotics, as are adverse effects on lipids and blood glucose, he continued.

Iloperidone (Fanapt), approved in 2009, is an oral atypical antipsychotic dosed at 12-24 mg/day b.i.d. The risk of hypotension makes it necessary to titrate to 12 mg/day over a 4-day period.

Weight gain and risk of extrapyramidal symptoms are lower than with many of the older atypical agents. However, prolongation of the QT interval occurs in a small percentage of patients, creating what is to this point still merely a theoretic concern about a possible increased risk of torsades de pointes. Nonetheless, the QT interval prolongation findings have resulted in insertion of a warning in the product labeling that iloperidone should be considered a second-line agent.

"To be honest, I think that the whole QT prolongation issue with our psychiatric medications has turned out to be a big exaggerated worry. We've seen very, very few problems with serious arrhythmias. The metabolic side effects with the atypical antipsychotic agents are a much more serious issue," Dr. Nasrallah asserted.

The last 2 years have also brought marketing approval of two new long-acting formulations of existing atypical antipsychotics: paliperidone palmitate (Invega Sustenna) and olanzapine pamoate (Zyprexa Relprevv). These long-acting products have an important role in patients with poor medication adherence, which Dr. Nasrallah called "a plague" in schizophrenia.

He said he routinely uses a long-acting agent from the get-go in patients who've committed a violent act during their first schizophrenic episode, because they tend to repeat the same symptoms in subsequent episodes.

Paliperidone palmitate is given in an initial 234-mg intramuscular loading dose in the deltoid muscle followed by 156 mg after 8 days. Thereafter, monthly maintenance dosing is given at 39-234 mg in either the gluteal or deltoid muscle. The drug is well tolerated overall, with no need for oral supplementation.

Long-acting olanzapine pamoate is a less practical drug; because of rare side effects, its administration must be followed by direct observation for about 3 hours with a crash cart nearby.

With the approval of three new atypical antipsychotic medications in the past 3 years, that makes a total of nine distinct drugs on the market today, some in multiple formulations. Is that redundancy? Not in Dr. Nasrallah's view.

"I'm happy that we have nine atypical antipsychotics on the market, because it turns out patients will respond to one but not another, and by trial and error we find out how to use these drugs. All of them work in about 70% of patients, but maybe a different 70% for each. So me-too drugs are useful," he said.

An audience member, noting that some of the newer atypical antipsychotic drugs cost $5,000 per year, asked Dr. Nasrallah how society can afford them.

"Don't get me started on pharmacoeconomics," Dr. Nazrallah said. "I am just so angry that the insurance companies somehow get away with discriminating against psychiatrists and psychiatric patients. When a hemophiliac needs a replacement factor that costs $100,000 per year, Medicaid, Medicare, and private insurance will pay it without blinking. But schizophrenia? No, $5,000 a year is too much. And then there are many cancers where it costs $40,000-$60,000 to prolong life by 6 months. They pay, and they don't make a big fuss about it. But they do make a big fuss about our patients and our drugs."

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