

CASE REPORT

Mania may be associated with modafinil in therapeutic doses

Patient: : Male (17 y/o)

Medications: Modafinil (Provigil), methylphenidate (Concerta)

Comment: A 17-year old boy, diagnosed with narcolepsy at the age of 14, was first prescribed modafinil (400 mg/day) for 1 year, switched to methylphenidate (40 mg/day) for 2 years, and then returned to modafinil (400 mg/day). The medication was switched due to complaints of irritability and lack of efficacy for treating the sleep attacks. At some point, the subject experienced manic symptoms characterized by increased irritability, flights of fancy and sexual excitation which caused friction with family members, and resulted in a severe fight.

When he off the psychostimulant medication (i.e., modafinil), the patient appeared sad, anhedonic and withdrawn. When the medication was switched back to modafinil (400 mg/day) the manic symptoms reoccurred, and the subject experienced "self-referential thinking" and suspiciousness. A full manic episode developed, which included insomnia, psychomotor agitation and mood-incongruent psychosis. The subject experienced delusions of persecution and visual hallucinations. He was then hospitalized and modafinil was discontinued. His mania required pharmacological treatment that began after written consent had been obtained from the patient and his parents.

According to the authors, this may be the first report of a patient experiencing mania while undergoing treatment with modafinil in therapeutic doses. Although an independent psychiatric disorder cannot be ruled out, the authors suggest that patients receiving modafinil and other psychostimulants for narcolepsy be carefully monitored. ■

Vorspan F, et al.: Mania in a boy treated with modafinil for narcolepsy. *Am J Psychiatry* 2005; 162(4):813-814.

[Editor's note: The case report as written is difficult to interpret as to the timing of the manic episodes. My understanding is that the first manic episode was on methylphenidate and the second episode was while on modafinil. — Henrietta L. Leonard, M.D.]

NEWS NOTES

FDA requests further data on anticonvulsants and suicide

The New York Times has reported that the Food and Drug Administration (FDA) has requested the manufacturers of epilepsy drugs to reexamine their clinical trial data to determine whether the drugs increase patients' risk of suicide. The request follows a petition by a personal injury attorney who claims that Pfizer's anticonvulsant Neurontin (gabapentin) resulted in a number of suicides and suicide attempts among his clients. Pfizer and 13 other manufacturers of epilepsy drugs have six months to analyze the results of their clinical trials. *The Update* will continue to monitor and report on these developments. [www.nytimes.com]

Methylphenidate transdermal patch for ADHD: positive clinical data

Results from two (7-week) clinical trials show that a methylphenidate transdermal system (MTS) was well tolerated in

treatment for children with attention-deficit hyperactivity disorder (ADHD). Both studies — a phase 2 study (N=79) and a phase 3 study (N=268) — examined MTS in children aged 6 to 12 years, previously diagnosed with ADHD. MTS (formerly referred to as METHYPATCH) is being developed by Shire Pharmaceuticals Group plc and Noven Pharmaceuticals Inc. According to Shire, the results demonstrate that "MTS has the potential to provide significant benefits for children with ADHD, especially those that have difficulty taking oral medications and those that find a once-a-day patch more appropriate for their lifestyle." The FDA will review an amendment, which includes the new trial results, to the product's New Drug Application within 6 months after submission. Further trial results will be released by Shire in May 2005. [www.shire.com]

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From the

FDA

✓ Tentative approvals for olanzapine generics

The FDA has given tentative approval to Teva Pharmaceutical Industries Ltd. and Mylan Laboratories for marketing a generic form of olanzapine in multiple strengths. Olanzapine is the generic equivalent of Eli Lilly's Zyprexa. Lilly holds the patent on Zyprexa until April 2011. However, Teva, as well as two other generic manufacturers, have challenged the validity of Lilly's patent. Ivax Corp. will be the first company to manufacture the generic version once Lilly's patent expires. [www.fda.gov]

✓ Non-approval of Lexapro for panic disorder

Forest Laboratories, Inc. reports that the FDA has issued a non-approval letter for the second time for the SSRI anti-depressant, Lexapro (escitalopram oxalate). This is in response to the company's reply to the FDA's initial non-approval letter. Forest Labs is now reviewing appropriate action to take with regard to the panic disorder submission. The drug is indicated for treatment of major depressive disorder and maintenance of major depressive disorder in adults. [www.fda.gov]

✓ Bolded warning for off-label Gabitril use

The FDA has announced that a bolded warning will be added to the labeling for Gabitril (tiagabine) to warn of the risk of seizures in patients without epilepsy being treated with this drug. Gabitril is indicated as adjunctive treatment in patients 12 years and older for partial seizures. The warning follows reports of the occurrence of seizures in more than 30 patients prescribed the drug for conditions other than epilepsy; these were primarily patients with psychiatric illnesses. The sponsor has agreed to issue a letter to healthcare providers and to undertake an educational campaign to discourage off label use. [www.fda.gov/cder/drug/advisory/gabitril.htm]