SPECIAL MESSAGE
STRATTERA: AN IMPORTANT UPDATE

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An article published in the Fall 2004 issue of this journal discussed a recently approved drug, Strattera, which is used for children and adults with ADHD. The advantages and disadvantages of this medication were discussed in detail. One of the main attributes of the drug was the fact that it was not a stimulant medication, but rather worked by blocking or slowing the reabsorption of norepinephrine, a brain chemical considered important in regulating attention, impulsivity and activity levels. Popular stimulant medications such as Ritalin, Adderall, Concerta, and Cylert had the potential for substance abuse, especially among at-risk populations. Also, some individuals with physical disabilities such as spasticity found that these popular medications exacerbated motor problems. As a result, Strattera seemed to be a logical alternative.

As noted in the original article, preliminary research from a number of medical investigators was somewhat brief, typically 10 weeks in duration with the longest study lasting 12 weeks. Eli Lilly and Company reported short-term clinical trials involving 6,000 patients. Since the introduction of the drug in 2002, Strattera has been prescribed to approximately two million individuals. This additional time frame and increased pool of patients taking Strattera has revealed additional side effects not previously reported in the original manuscript including: constipation, nausea, urinary hesitation and/or urinary retention, and dysmenorrhea (Hankin, 2005). By far, the most significant previously unreported side effect is liver injury.

CONSUMER WARNING

Recently, the Food and Drug Administration (FDA) requested that Eli Lilly and Company include a "bolded" warning informing users of potential for liver damage ("Warning of," 2005). Eli Lilly complied with this request in December, 2004 and posted a "bolded" warning on this product to inform consumers of potential liver damage. In part this warning as reported by Hankin (2005) states,

> STRATTERA can cause severe liver injury in rare cases. . .there have been two reported cases of markedly elevated hepatic enzymes and bilirubin, in the absence of other obvious explanatory factors. . .In one patient, liver injury, manifested by elevated hepatic enzymes (up to 40 X upper limit of normal (ULN)) and jaundice (bilirubin up to 12 X ULN), recurred upon rechallenge, and was followed by recovery upon drug discontinuation providing evidence that STRATTERA caused the liver injury. Such reactions may occur several months after therapy is started. . .Because of probable underreporting, it is impossible to provide an accurate estimate of the true incidence of these events. The patients described above recovered from their liver injury, and did not require a liver transplant. However, in a small percentage of patients, severe drug-related liver injury may progress to acute liver failure resulting in death or the need for a liver transplant. (pp. 2–3)

PATIENT CAUTIONARY ADVICE

Individuals using Strattera should be aware of the following symptoms associated with liver injury: pruritus, jaundice, dark urine, pain on the upper right side of the stomach, unexplained nausea, and unexplained flu-like symptoms (Aschenbreener, 2005, "Recent changes", 2005). Persons experiencing any of these symptoms should immediately report them to the prescriber.

PHYSICIAN UPDATES

UNITED STATES

In addition to the bolded patient statement, a "Dear Health Care Professional" letter dated December 21, 2004, included many of the same warnings and noted that liver injury connected with Strattera was idiosyncratic and unpredictable (Eisenberg, 2004). Physicians were encouraged to

promptly investigate the vague signs and symptoms of liver damage and report problems to Eli Lilly and Company or the FDA.

UNITED KINGDOM

The British equivalent of the FDA, the Department of Health, Social Services, and Public Safety, also issued a "Dear Colleague" letter on February 2, 2005 which noted 41 cases worldwide of hepatic disorders associated with Strattera (Duff, 2005). The estimated risk is 1 in 50,000 or less. The advice to physicians is very similar to that given in the United States. An attached information sheet for parents and patients reported that Strattera will be under constant scrutiny. "This particular safety issue is being actively investigated and any new information will be urgently evaluated and, if necessary, new guidance will be issued" (p. 3).

DISCUSSION

As can be seen above, there are new concerns about the use of Strattera after it has been prescribed to two million people over a four year period. Severe liver injury has been seen in 2 people in the United States and 41 persons worldwide. Although these numbers appear to be quite small, the pharmaceutical company states that because of probable underreporting the actual number of affected persons is currently unknown.

Parents, teachers, and support personnel should not overreact to these reports, but should be judicious in watching for typical signs of hepatic or liver problems: itchy skin, abdominal pain, yellowing of the eyes and skin, discolored urine, and flu symptoms coupled with nausea. If any of these signs are present following the administration of Strattera, the physician should be contacted immediately. Additionally, parents should discuss this new health risk with the child's physician during routine checkups. This might be especially important for children with other health impairments.

In the original manuscript the authors noted that because a paucity of research existed in the professional literature, longitudinal studies were recommended. This recommendation seems even more important now. Additionally, because this side effect appears to be an idiosyncratic phenomenon related to the use of Strattera, medical researchers should investigate possible correlations between liver damage and other contributing factors. One has to remember that Strattera continues to be an important tool in the treatment of ADHD and risk needs to be balanced with the benefits.

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