Premature Ejaculation Drug Waits in the Pipeline

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PARIS — Investigators have reported that an experimental on-demand drug for premature ejaculation was well tolerated in a 9-month open-label extension of two 12-week randomized controlled trials supporting its effectiveness.

A total of 962 (54.2%) of 1,774 participants stayed on dapoxetine hydrochloride for a full year, according to a poster presented by Dr. Wayne Hellstrom at the annual congress of the European Association of Urology.

The 812 dropouts (45.8%) included 227 men (12.8%) who withdrew because of lack of efficacy and 119 (6.7%) who quit because of adverse events. Another 175 men (9.9%) were lost to follow-up.

"People move. People have different reasons to drop out. For a 12-month study to maintain 54% of the patients on a drug is pretty good," Dr. Hellstrom, a professor of urology and chief of andrology at Tulane University in New Orleans, told a physician in the audience who questioned the study's dropout rate during a discussion of the poster.

Dapoxetine's developer, Alza Corporation, announced in October 2005 that the Food and Drug Administration had sent a "not approvable" letter in response to Alza's new drug application for dapoxetine. Dr. Hellstrom said that he did not know the reason for the rejection but that he had been told the company plans to reapply.

No medications are currently approved for premature ejaculation in the United States or in Europe, according to Dr. Hellstrom. He said selective serotonin reuptake inhibitors are sometimes prescribed.

"The problem is there are side effects," he said. "Patients have to take [SSRIs] for 2 weeks to get inhibition."

Phosphodiesterase-5 inhibitors also are used occasionally, he said, with the qualification that there is little evidence to support use of erectile dysfunction drugs for premature ejaculation.

Dapoxetine is a serotonin transporter inhibitor designed to increase intravaginal ejaculatory latency time (IELT) with a single dose taken 1-3 hours before intercourse.

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DR. HELLSTROM

The initial 12-week double-blind multicenter studies enrolled men 18 years of age and older who were in a stable, monogamous relationship for at least 6 months and met diagnostic criteria for premature ejaculation. All had an IELT of 2 minutes or less as measured with a stopwatch by their female partners in at least 75% of intercourse episodes during a 2-week period. In self-reports, the men characterized their premature ejaculation as moderate or severe.

The men were randomized to 30-mg or 60-mg doses of dapoxetine or placebo in the initial trials, which reported that dapoxetine was effective.

The 9-month open-label extension study enrolled men from September 2003 to April 2005. All participants started on a 60-mg dose 1-3 hours before intercourse, regardless of the treatment to which they were assigned in the first set of trials.

Investigators were allowed to reduce the dapoxetine dose to 30 mg in patients who did not tolerate 60 mg or requested a lower dose. Adverse events led to reduction of the dose for 192 men. In two other men, the dose was lowered by request.

The most common adverse events during the extension study were nausea in 265 men (14.9%), dizziness in 90 men (5.1%), and diarrhea in 82 men (4.6%). Other side effects occurring in 2% or more of the population were headache, somnolence, insomnia, dyspepsia, and asthenia.

Three men had serious treatment-related adverse events: one case each of syncope, seizure, and a syncopal episode.

"With the 9-month extension, there wasn't any difference from the first 3 months," Dr. Hellstrom said, reporting that no new safety concerns emerged with longer use of dapoxetine.

He said he serves on the speakers' bureau and is a consultant to Alza Corporation, which supported the study. ■

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