Study Scrutinizes Safety of Teen Contraceptive Use

**By Elizabeth Meacham**

**Senior Writer**

**Rockville, Md. —** No new safety concerns were raised by a review of adverse events reported during a recent 1-year period in adolescents taking a combination oral contraceptive, according to J.W. Scott, M.D., director of the Food and Drug Administration’s division of pediatric drug development.

The FDA’s review of adverse events reported for Ortho Tri-Cyclen and Ortho Tri-Cyclen Lo, which contain norgestimate and ethinyl estradiol, was conducted during December 2003 and January 2004, the year after the FDA granted marketing exclusivity to the drug. Exclusivity is granted to a drug when companies perform pediatric studies of the product in exchange for a 6-month extension on the drug’s patent.

In this case, the manufacturer, Ortho-McNeil Pharmaceutical Inc., conducted a placebo-controlled study to determine whether the OC improved bone density in adolescent girls with anorexia nervosa. The study showed no differences from placebo in increases in hip and lumbar spine bone mineral density after 1 year of treatment.

The second case involved a 20-year-old who had a vaginal delivery 5 months earlier and who at 3 months post partum was breast-feeding and amenorrheic. She presented with visual adverse events, which are not mentioned in the label of Ortho Tri-Cyclen, and convulsions, an adverse event that is not in the label.

There were four hospitalizations, which included the two in utero exposures. The other two hospitalizations were in a 16-year-old with benign intracranial hypertension, an increase in cerebrospinal fluid pressure, and a visual field defect; and in a 14-year-old who had cerebral thrombosis and alprazolam while pregnant. The second case involved a 19-year-old who had a vaginal delivery 5 months earlier and who at 3 months post partum was breast-feeding and amenorrheic.

The fourth case involved a 19-year-old who had a vaginal delivery 5 months earlier and who at 3 months post partum was breast-feeding and amenorrheic. She began using DMPA for contraception at that time, and 2 months later, she presented with bleeding and cramping. As with the first three cases, examination revealed a large amount of tissue at the cervical os.

The findings in each case were consistent with decidual cast expulsion, and all patients had a negative result on a pregnancy test. The removal of the protruding tissue resulted in symptom resolution, said Dr. Scott of the University of Colorado, Denver.

Because decidual casts are rare, “we don’t really have a great idea of what elements are needed in order to form a decidual cast,” he said.

**Dr. Scott**

In theory, however, decidual cast formation can be expected when prolonged estrogen-only stimulation of the endometrium, and thus endometrial proliferation. The fourth patient also may have had prolonged estrogen production with resumption of ovarian estrogen production late in breast-feeding.

DMPA treatment in these patients would then have resulted in a high level of progestrone exposure followed by a gradual decline in progesterone levels that might have led to the decidual casts, he said.

In most of these cases, the decidual casts were, understandably, very frightening for the patient and/or parent, he added.

For this reason, as well as to fully inform patients about the potential effects of DMPA and to promote treatment compliance, patient counseling should include discussion of decidual cast expulsion as a rare side effect associated with the drug.

Furthermore, because 1% of DMPA failures are ectopic pregnancies (albeit rare, not a known event), the FDA noted the potential of progesterone exposure, leading to a thicker endometrial layer. When the progesterone levels fall, the likelihood of decidual cast formation is increased.

Although these cases had varying scenarios, it is possible that similar hormonal events led to the decidual cast formation and passage, he explained.

Dr. Temeck reported the data at a meeting of the FDA’s Pediatric Advisory Committee. The Best Pharmaceuticals for Children Act requires that the FDA’s Office of Pediatric Therapeutics review postmarketing adverse event reports made to the FDA’s MedWatch adverse event reporting system during the year after a drug receives market exclusivity. These reports are then referred to the Pediatric Advisory Committee for a review.

The uses of Ortho Tri-Cyclen for females 16 years of age and younger include dysfunctional uterine bleeding and acne, she said. During the postexclusivity period (Dec. 18, 2003, through Jan. 18, 2005) there were 14 unduplicated pediatric adverse event reports associated with Ortho Tri-Cyclen, including 11 serious reports and 6 deaths.

The 14 reports included 12 cases in adolescent girls and 2 cases involving infants that had been exposed in utero. Adverse events that were reported more than once were headaches and metrorrhagia, according to the report. The 14 reports included 12 cases in adolescent girls and 2 cases involving infants that had been exposed in utero. Adverse events that were reported more than once were headaches and metrorrhagia, according to the report.

The investigators said that the reviewers had to consider that although DMPA is not a known cause of serious adverse events, menorrhagia may occur in young patients associated with ectopic pregnancy and increased risk of birth defects.

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