

Risk of pseudotumor cerebri added to labeling for gonadotropin-releasing hormone agonists

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from the Food and Drug Administration

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The Food and Drug Administration (FDA) has added a warning about the risk of pseudotumor cerebri (idiopathic intracranial hypertension) to the labeling for gonadotropin-releasing hormone (GnRH) agonists that are approved for the treatment of central precocious puberty in pediatric patients. These products include Lupron Depot-Ped (leuprolide acetate), Fensolvi (leuprolide acetate), Synarel (nafarelin), Supprelin LA (histrelin) and Triptodur (triptorelin).

The new warning includes recommendations to monitor patients taking GnRH agonists for signs and symptoms of pseudotumor cerebri, including headache, papilledema, blurred or loss of vision, diplopia, pain behind the eye or pain with eye movement, tinnitus, dizziness and nausea.

The FDA assessed the potential risk of pseudotumor cerebri with use of GnRH agonists in pediatric patients by reviewing post-marketing safety data submitted by the GnRH agonist manufacturers, searching the FDA Adverse Event Reporting System and conducting a literature search.

Six cases were identified that supported a plausible association between GnRH agonist use and pseudotumor cerebri. All six cases were reported in birth-assigned females ages 5 to 12 years. Five were undergoing treatment for central precocious puberty and one for transgender care. The onset of pseudotumor cerebri symptoms ranged from three to 240 days after GnRH agonist initiation.

Symptoms included visual disturbances (n=5), headache or vomiting (n=5), papilledema (n=3), blood pressure increase (n=1) and abducens neuropathy (n=1). Treatments included lumbar puncture (n=3), acetazolamide therapy (n=5) and ventricular peritoneal shunting (n=1).

At the time of the FDA's review, symptoms had resolved in three patients, were resolving in one patient, had not resolved in one patient, and one patient's status was unknown. GnRH agonist therapy was discontinued in three patients; the status of continued therapy was unknown for the remaining three patients.

The incidence rate of pseudotumor cerebri associated with GnRH agonist use in pediatric patients could not be reliably established due to the small number of cases and data limitations.

The FDA's Office of Pediatric Therapeutics (OPT), Division of Pediatrics and Maternal Health (DPMH) and Division of General Endocrinology (DGE) contributed to this article. OPT resides in the Office of Clinical Policy and Programs in the Office of the Commissioner. DPMH resides in the Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine. DGE resides within the Office of Cardiology, Hematology,

Endocrinology and Nephrology. Both DPMH and DGE reside within the Office of New Drugs in the Center for Drug Evaluation and Research.

Resource

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