

ing, respiratory distress, and a muffled voice. The classic symptoms of neck stiffness and bulging of the posterior pharyngeal wall are present in fewer than 50% of patients.

On physical examination, the child can present with anterolateral neck swelling, hyperextension of the neck, or an enlarged cervical lymph node, she explained at the meeting, which was sponsored by the university.

Imaging is needed to confirm a diagnosis of a retropharyngeal abscess. A lateral x-ray of the neck area may show soft tissue swelling, and a CT scan of the neck can be helpful if the x-ray findings are uncertain and the clinical suspicion is high.

Immediate treatment includes airway maintenance, pain management, and hydration before admitting the child to the hospital. Consult an ear, nose, and

throat specialist when the diagnosis is confirmed or if the child has an obstructed airway. The abscess treatment plan includes incising and draining the abscess, and treating the child with parenteral antibiotics, such as clindamycin or a combination of sulbactam and ampicillin.

“Prompt diagnosis and treatment of pharyngitis or upper respiratory infections will generally prevent retropharyngeal abscess,” said Dr. Figueira. This condition can [also] lead to laryngeal edema with possible airway obstruction, mediastinitis, and aspiration pneumonia, but with prompt treatment a patient can make a full recovery.” ■

A 35-year review of cases showed 50% of patients with retropharyngeal abscesses were younger than 3 years and that 71% were younger than 6 years.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Amitiza. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Voluntary reports of adverse reactions occurring with the use of Amitiza include the following: syncope, malaise, increased heart rate, muscle cramps or muscle spasms, rash, and asthenia.

7 DRUG INTERACTIONS

Based upon the results of *in vitro* human microsome studies, there is low likelihood of drug–drug interactions. *In vitro* studies using human liver microsomes indicate that cytochrome P450 isoenzymes are not involved in the metabolism of lubiprostone. Further *in vitro* studies indicate microsomal carbonyl reductase may be involved in the extensive biotransformation of lubiprostone to the metabolite M3 (See *Pharmacokinetics, Metabolism* [12.3]). Additionally, *in vitro* studies in human liver microsomes demonstrate that lubiprostone does not inhibit cytochrome P450 isoforms 3A4, 2D6, 1A2, 2A6, 2B6, 2C9, 2C19, or 2E1, and *in vitro* studies of primary cultures of human hepatocytes show no induction of cytochrome P450 isoforms 1A2, 2B6, 2C9, and 3A4 by lubiprostone. No additional drug–drug interaction studies have been performed. Based on the available information, no protein binding–mediated drug interactions of clinical significance are anticipated.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic effects: Pregnancy Category C. [See *Warnings and Precautions* (5.1).]

Teratology studies with lubiprostone have been conducted in rats at oral doses up to 2000 mcg/kg/day (approximately 332 times the recommended human dose, based on body surface area), and in rabbits at oral doses of up to 100 mcg/kg/day (approximately 33 times the recommended human dose, based on body surface area). Lubiprostone was not teratogenic in rats or rabbits. In guinea pigs, lubiprostone caused fetal loss at repeated doses of 10 and 25 mcg/kg/day (approximately 2 and 6 times the recommended human dose, respectively, based on body surface area) administered on days 40 to 53 of gestation.

There are no adequate and well-controlled studies in pregnant women. However, during clinical testing of Amitiza at 24 mcg twice daily, four women became pregnant. Per protocol, Amitiza was discontinued upon pregnancy detection. Three of the four women delivered healthy babies. The fourth woman was monitored for 1 month following discontinuation of study drug, at which time the pregnancy was progressing as expected; the patient was subsequently lost to follow-up.

Amitiza should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. If a woman is or becomes pregnant while taking the drug, the patient should be apprised of the potential hazard to the fetus.

8.3 Nursing Mothers

It is not known whether lubiprostone is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from lubiprostone, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been studied.

8.5 Geriatric Use

The efficacy of Amitiza in the elderly (≥ 65 years of age) subpopulation was consistent with the efficacy in the overall study population. Of the total number of constipated patients treated in the dose-finding, efficacy, and long-term studies of Amitiza, 15.5% were ≥ 65 years of age, and 4.2% were ≥ 75 years of age. Elderly patients taking Amitiza (any dosage) experienced a lower incidence rate of associated nausea compared to the overall study population taking Amitiza (18% vs. 29%, respectively).

8.6 Renal Impairment

Amitiza has not been studied in patients who have renal impairment.

8.7 Hepatic Impairment

Amitiza has not been studied in patients who have hepatic impairment.

10 OVERDOSAGE

There have been two confirmed reports of overdosage with Amitiza. The first report involved a 3-year-old child who accidentally ingested 7 or 8 capsules of 24 mcg of Amitiza and fully recovered. The second report was a study patient who self-administered a total of 96 mcg of Amitiza per day for 8 days. The patient experienced no adverse reactions during this time. Additionally, in a Phase 1 cardiac repolarization study, 38 of 51

patients given a single oral dose of 144 mcg of Amitiza (6 times the recommended dose) experienced an adverse event that was at least possibly related to the study drug. Adverse reactions that occurred in at least 1% of these patients included the following: nausea (45%), diarrhea (35%), vomiting (27%), dizziness (14%), headache (12%), abdominal pain (8%), flushing/hot flash (8%), retching (8%), dyspnea (4%), pallor (4%), stomach discomfort (4%), anorexia (2%), asthenia (2%), chest discomfort (2%), dry mouth (2%), hyperhidrosis (2%), and syncope (2%).

16 HOW SUPPLIED/STORAGE AND HANDLING

Amitiza is available as an oval, orange, soft gelatin capsule with “SPI” printed on one side. Each capsule contains 24 mcg of lubiprostone. Amitiza is available as follows:

- Bottles of 100 (NDC 64764-240-10)
- Bottles of 60 (NDC 64764-240-60)

Store at 25°C (77°F); excursions permitted to 15°–30°C (59°–86°F). PROTECT FROM EXTREME TEMPERATURES.

17 PATIENT COUNSELING INFORMATION

17.1 Dosing Instructions

Patients should take a single 24 mcg capsule of Amitiza twice daily with food or a meal. The capsule should be taken once in the morning and once in the evening daily as prescribed. Physicians and patients should periodically assess the need for continued treatment with Amitiza.

17.2 Nausea and Diarrhea

Patients should take Amitiza with food or a meal to reduce symptoms of nausea. Patients on treatment who experience severe nausea or diarrhea should inform their physician.

Marketed by:

Sucampo Pharmaceuticals, Inc., Bethesda, MD 20814

and

Takeda Pharmaceuticals America, Inc., Deerfield, IL 60015

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Risk Behaviors Drive Up HIV In Adolescents

BY NANCY WALSH

New York Bureau

BOSTON — The adolescent HIV-1 epidemic as reflected in a multisite cohort of U.S. youth is changing from one of vertically transmitted infection to one where infection is acquired through risk behaviors, posing new challenges for providers and the health care system, said Dr. Allison L. Agwu in a poster session at the 15th Conference on Retroviruses and Opportunistic Infections.

The HIV Research Network, a consortium of 21 clinical sites providing primary HIV care, includes 684 patients aged 12–24 years. Vertical transmission was the source of infection in 227 patients and risk behaviors accounted for 457 cases, said Dr. Agwu of Johns Hopkins University, Baltimore.

Analysis of data from this cohort showed patients infected through risk behaviors are older, with a median age of 22 years, compared with a median age of 15 years in vertical-transmission patients. They are also more likely to be male. Of the risk-behavior patients, 292 (64%) are male, as are 108 (48%) of the vertical-transmission patients.

Risk behaviors comprised men having sex with men (51%), unprotected heterosexual activity (45%), and IV drug use (4%).

The median CD4 count in the risk-behavior group was 492 cells/mm³, whereas that in the vertical-transmission group was 660 cells/mm³. The median HIV RNA level in the risk-behavior group was 6,700 copies/mL, compared with 400 copies/mL in the vertical-transmission group.

Despite this worse immune suppression and higher levels of viremia in the risk-behavior patients, they were less likely to be on highly active antiretroviral therapy (HAART) (43% vs. 88%). Those infected through risk behaviors also had significantly fewer outpatient visits, averaging five visits a year, whereas vertical-transmission patients averaged seven visits.

Rates of hospitalization did not differ, at 19/100 patient-years in the risk-behavior group and 17/100 patient-years in the vertical-transmission group, Dr. Agwu reported at the meeting, sponsored by the Foundation for Retrovirology and Human Health and the Centers for Disease Control and Prevention. Other aspects of treatment also did not differ significantly between the two groups. For example, 89% of those meeting the criteria for prophylaxis against *Pneumocystis carinii* pneumonia in the risk-behavior group received prophylaxis, as did 80% of vertical-transmission patients.

Differences in psychosocial risk factors between the two groups might account for the varying rates of HAART use, Dr. Agwu said in an interview. “[We’ll] focus on deciphering patient and provider barriers to HAART initiation in the risk-behavior group to institute appropriate interventions.” She added that the number of risk behavior patients in need of treatment is likely to grow as the Centers for Disease Control and Prevention’s recommendation of universal opt-out testing is implemented. ■