

# Kids Highly Vulnerable to Radiation in Imaging

BY JANE SALODOF MACNEIL  
Southwest Bureau

SCOTTSDALE, ARIZ. — Radiation exposure from the diagnostic imaging of children greatly increases their risk of cancer and death decades later, according to speakers at a pediatric update sponsored by Phoenix Children's Hospital.

Dr. Thomas L. Slovis and Dr. Alan H. Friedman urged pediatricians to be judicious, limiting their use of chest x-rays

and computerized tomography to essential studies. They also called on pediatricians to insist that radiologists adjust radiation doses to minimize future harm to children.

Among the alarming statistics reported in their separate talks were the following: ▶ A 1-year-old infant is 10-15 times as likely to develop malignancy as is a 50-year-old adult given the same dose of radiation, according to the International Commission on Radiological Protection.

▶ The equivalent natural-radiation exposure ranges from 2.4 days of natural exposure during one chest x-ray to 4.3 years of natural exposure during one 30-minute cardiac catheterization. Within this range are one upper-gastrointestinal x-ray (equivalent to 1 year of natural exposure), one barium enema (equivalent to 2.3 years), and one abdominal CT scan (equivalent to 3.3 years).

▶ The risk of dying of complications from an abdominal CT scan performed in

the first year of life is 1:1,000. This is greater than the risk of death from a bicycle accident, drowning, or a medical complication, according to the National Safety Council.

▶ Low doses of radiation comparable to a CT dose are associated with excess cancers and excess deaths in an ongoing 50-year study of 50,000 atomic bomb survivors (Radiation Research 2000:154:178-86).

The issue is not whether to image, but when and how often and which test to use, said Dr. Friedman, director of the pediatric echocardiography laboratory at Yale University, New Haven, Conn.

"If we're not careful and thoughtful in the use of the technology, we may be exposing our youngest and most vulnerable



**"We may be exposing our ... most vulnerable patients to dangerous doses of radiation."**

DR. FRIEDMAN

patients to potentially dangerous and worrisome doses of radiation," he said in an interview. "It may not have an effect in the short term, but we may really start to realize deleterious effects decades down the road."

Along with more judicious use of tests, pediatricians should ask radiologists whether they tailor radiation doses for children, said Dr. Slovis, of the division of pediatric imaging at Wayne State University, Detroit.

He advocated wider application of the concept of ALARA ("as low as reasonably achievable") to radiation dosing in children. "You want the proper dose. If the dose is too low, you can't make the diagnosis," he said.

Various factors make children more susceptible to radiation. Dr. Friedman listed tissue weighting, the exposure of more or

*Continued on following page*

## How to Lower the Risk of Radiation

- ▶ Reduce the number of multiple scans and procedures.
- ▶ Reduce the length of time the patient is in the scanner.
- ▶ Use bismuth shields, which reduce radiation exposure by up to 67% and don't significantly affect imaging.
- ▶ Limit exposure/coverage to the physical area necessary for addressing the clinical question.
- ▶ Do not repeat studies too early or too often.
- ▶ Discuss the risks with the patients and parents.
- ▶ Consider MRI or ultrasound studies whenever possible.

Source: Dr. Friedman

Brief Summary of Prescribing Information (Nos. 1541, 1543, 1544, 3046, 7309, 7311) 03-5366-R24-Brl. Rev. July, 2004

**PREVACID®** (lansoprazole) Delayed-Release Capsules

**PREVACID®** (lansoprazole) For Delayed-Release Oral Suspension

**PREVACID® SoluTab™** (lansoprazole) Delayed-Release Orally Disintegrating Tablets

**Rx only**

**PREVACID Delayed-Release Capsules, PREVACID SoluTab Delayed-Release Orally Disintegrating Tablets and PREVACID For Delayed-Release Oral Suspension are indicated for:**

**Short-Term Treatment (4 weeks) of Active Duodenal Ulcer**

**H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence**

Triple Therapy: PREVACID/amoxicillin/clarithromycin

Dual Therapy: PREVACID/amoxicillin

**Who are either allergic or intolerant to clarithromycin or in whom resistance to clarithromycin is known or suspected.**

**Maintenance of Healed Duodenal Ulcers**

Controlled studies do not extend beyond 12 months.

**Short-Term Treatment (up to 8 weeks) of Active Benign Gastric Ulcer**

**Healing of NSAID-Associated Gastric Ulcer**

In patients with a history of a documented gastric ulcer who require the use of an NSAID. Controlled studies did not extend beyond 8 weeks.

**Risk Reduction of NSAID-Associated Gastric Ulcer**

In patients with a history of a documented gastric ulcer who require the use of an NSAID. Controlled studies did not extend beyond 12 weeks.

**Gastroesophageal Reflux Disease (GERD)**

Short-Term Treatment of Symptomatic GERD

Short-Term Treatment (up to 8 weeks) of Erosive Esophagitis

For patients who do not heal with PREVACID for 8 weeks (5-10%), it may be helpful to give an additional 8 weeks of treatment. If there is a recurrence of erosive esophagitis an additional 8-week course of PREVACID may be considered.

**Maintenance of Healing of Erosive Esophagitis**

Controlled studies did not extend beyond 12 months.

**Pathological Hypersensitivity Conditions Including Zollinger-Ellison Syndrome**

**CONTRAINDICATIONS**

PREVACID is contraindicated in patients with known hypersensitivity to any component of the formulation of PREVACID.

Amoxicillin is contraindicated in patients with a known hypersensitivity to any penicillin.

Clarithromycin is contraindicated in patients with a known hypersensitivity to clarithromycin, erythromycin, and any of the macrolide antibiotics.

Concomitant administration of clarithromycin with cisapride, pimozide, astemizole, or terfenadine is contraindicated. There have been post-marketing reports of drug interactions when clarithromycin and erythromycin are co-administered with cisapride, pimozide, astemizole, or terfenadine resulting in cardiac arrhythmias (QT prolongation, ventricular tachycardia, ventricular fibrillation, and torsades de pointes) most likely due to inhibition of metabolism of these drugs by erythromycin and clarithromycin. Fatalities have been reported.

(Please refer to full prescribing information for amoxicillin and clarithromycin before prescribing.)

**WARNINGS**

CLARITHROMYCIN SHOULD NOT BE USED IN PREGNANT WOMEN EXCEPT IN CLINICAL CIRCUMSTANCES WHERE NO ALTERNATIVE THERAPY IS APPROPRIATE. IF PREGNANCY OCCURS WHILE TAKING CLARITHROMYCIN, THE PATIENT SHOULD BE APPRISED OF THE POTENTIAL HAZARD TO THE FETUS. (SEE WARNINGS IN PRESCRIBING INFORMATION FOR DRUG CLARITHROMYCIN.)

**Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clarithromycin and amoxicillin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.**

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis."

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more apt to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens.

There have been well-documented reports of individuals with a history of penicillin hypersensitivity reactions who have experienced severe hypersensitivity reactions when treated with a cephalosporin. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, amoxicillin should be discontinued and the appropriate therapy instituted.

**SERIOUS ANAPHYLACTIC REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE, OXYGEN, INTRAVENOUS STEROIDS, AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, SHOULD ALSO BE ADMINISTERED AS INDICATED.**

**PRECAUTIONS**

**General**

Symptomatic response to therapy with lansoprazole does not preclude the presence of gastric malignancy.

**Information for Patients**

PREVACID is available as a capsule, orally disintegrating tablet and oral suspension, and is available in 15 mg and 30 mg strengths. Directions for use specific to the route and available methods of administration for each of these dosage forms is presented below. PREVACID should be taken before eating. PREVACID products SHOULD NOT BE CRUSHED OR CHEWED.

**Phenylketonurics: Contains Phenylalanine 2.5 mg per 15 mg Tablet and 5.1 mg per 30 mg Tablet.**

**Administration Options**

**1. PREVACID Delayed-Release Capsules**

PREVACID Delayed-Release Capsules should be swallowed whole.

Alternatively, for patients who have difficulty swallowing capsules, PREVACID Delayed-Release Capsules can be opened and administered as follows:

- Open capsule.
- Sprinkle intact granules on one tablespoon of either applesauce, ENSURE® pudding, cottage cheese, yogurt or strained pears.
- Swallow immediately.

PREVACID Delayed-Release Capsules may also be emptied into a small volume of either apple juice, orange juice or tomato juice and administered as follows:

- Open capsule.
- Sprinkle intact granules into a small volume of either apple juice, orange juice or tomato juice (60 mL – approximately 2 ounces).
- Mix briefly.
- Swallow immediately.

To ensure complete delivery of the dose, the glass should be rinsed with two or more volumes of juice and the contents swallowed immediately.

USE IN OTHER FOODS AND LIQUIDS HAS NOT BEEN STUDIED CLINICALLY AND IS THEREFORE NOT RECOMMENDED.

**2. PREVACID SoluTab Delayed-Release Orally Disintegrating Tablets**

PREVACID SoluTab should not be chewed. Place the tablet on the tongue and allow it to disintegrate, with or without water, until the particles can be swallowed. The tablet typically disintegrates in less than 1 minute.

Alternatively, for children or other patients who have difficulty swallowing tablets, PREVACID SoluTab can be delivered in two different ways.

**PREVACID SoluTab – Oral Syringe**

For administration via oral syringe, PREVACID SoluTab can be administered as follows:

- Place a 15 mg tablet in oral syringe and draw up approximately 4 mL of water, or place a 30 mg tablet in oral syringe and draw up approximately 10 mL of water.
- Shake gently to allow for a quick dispersal.
- After the tablet has dispersed, administer the contents within 15 minutes.
- Refill the syringe with approximately 2 mL (5 mL for the 30 mg tablet) of water, shake gently, and administer any remaining contents.

**PREVACID SoluTab – Nasogastric Tube Administration (≥ 8 French)**

For administration via a nasogastric tube, PREVACID SoluTab can be administered as follows:

- Place a 15 mg tablet in a syringe and draw up 4 mL of water, or place a 30 mg tablet in a syringe and draw up 10 mL of water.
- Shake gently to allow for a quick dispersal.
- After the tablet has dispersed, inject through the nasogastric tube into the stomach within 15 minutes.
- Refill the syringe with approximately 5 mL of water, shake gently, and flush the nasogastric tube.

**3. PREVACID For Delayed-Release Oral Suspension**

PREVACID For Delayed-Release Oral Suspension should be administered as follows:

- Open packet.
- To prepare a dose, empty the packet contents into a container containing 2 tablespoons of WATER. DO NOT USE OTHER LIQUIDS OR FOODS.
- Stir well, and drink immediately.
- If any material remains after drinking, add more water, stir, and drink immediately.
- This product should not be given through enteral administration tubes.

**Drug Interactions**

Lansoprazole is metabolized through the cytochrome P<sub>450</sub> system, specifically through the CYP3A and CYP2C19 isozymes. Studies have shown that lansoprazole does not have clinically significant interactions with other drugs metabolized by the cytochrome P<sub>450</sub> system, such as warfarin, antipyrine, indomethacin, ibuprofen, phenytoin, propranolol, prednisone, diazepam, or clarithromycin in healthy subjects. These compounds are metabolized through various cytochrome P<sub>450</sub> isozymes including CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A. When lansoprazole was administered concomitantly with theophylline (CYP1A2, CYP3A), a minor increase (10%) in the clearance of theophylline was seen. Because of the small magnitude and the direction of the effect on theophylline clearance, this interaction is unlikely to be of clinical concern. Nonetheless, individual patients may require additional titration of their theophylline dosage when lansoprazole is started or stopped to ensure clinically effective blood levels.

In a study of healthy subjects neither the pharmacokinetics of warfarin enantiomers nor prothrombin time were affected following single or multiple 60 mg doses of lansoprazole. However, there have been reports of increased International Normalized Ratio (INR) and prothrombin time in patients receiving proton pump inhibitors, including lansoprazole, and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with proton pump inhibitors and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time.

Lansoprazole has also been shown to have no clinically significant interaction with amoxicillin. In a single-dose crossover study examining lansoprazole 30 mg and omeprazole 20 mg each administered alone and concomitantly with sucralfate 1 gram, absorption of the proton pump inhibitors was delayed and their bioavailability was reduced by 17% and 16%, respectively, when administered concomitantly with sucralfate. Therefore, proton pump inhibitors should be taken at least 30 minutes prior to sucralfate. In clinical trials, antacids were administered concomitantly with PREVACID Delayed-Release Capsules, and did not interfere with its effect.

Lansoprazole causes a profound and long-lasting inhibition of gastric acid secretion; therefore, it is theoretically possible that lansoprazole may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g., ketoconazole, ampicillin esters, iron salts, digoxin).

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

In two 24-month carcinogenicity studies, Sprague-Dawley rats were treated orally with doses of 5 to 150 mg/kg/day, about 1 to 40 times the exposure on a body surface (mg/m<sup>2</sup>) basis, of a 50-kg person of average height (1.46 m<sup>2</sup> body surface area) given the recommended human dose of 30 mg/day (22.2 mg/m<sup>2</sup>). Lansoprazole produced dose-related gastric enterochromaffin-like (ECL) cell hyperplasia and ECL cell carcinoids in both male and female rats. It also increased the incidence of intestinal metaplasia of the gastric epithelium in both sexes. In male rats, lansoprazole produced a dose-related increase of testicular interstitial cell adenomas. The incidence of these adenomas in rats receiving doses of 15 to 150 mg/kg/day (4 to 40 times the recommended human dose based on body surface area) exceeded the low background incidence (range = 1.4 to 10%) for this strain of rat. Testicular interstitial cell adenoma also occurred in 1 of 30 rats treated with 50 mg/kg/day (13 times the recommended human dose based on body surface area) in a 1-year toxicity study.

In a 24-month carcinogenicity study, CD-1 mice were treated orally with doses of 15 to 600 mg/kg/day, 2 to 80 times the recommended human dose based on body surface area. Lansoprazole produced a dose-related increase of incidence of gastric ECL cell hyperplasia. It also produced an increased incidence of liver tumors (hepatocellular adenoma plus carcinoma). The tumor incidences in male mice treated with 300 and 600 mg/kg/day (40 to 80 times the recommended human dose based on body surface area) and female mice treated with 150 to 600 mg/kg/day (20 to 80 times the recommended human dose based on body surface area) exceeded the ranges of background incidences in historical controls for this strain of mice. Lansoprazole produced adenoma of rete testis in male mice receiving 75 to 600 mg/kg/day (10 to 80 times the recommended human dose based on body surface area).

Lansoprazole was not genotoxic in the Ames test, the *ex vivo* rat hepatocyte unscheduled DNA synthesis (UDS) test, the *in vivo* mouse micronucleus test or the rat bone marrow cell chromosomal aberration test. It was positive in *in vitro* human lymphocyte chromosomal aberration assays.

Lansoprazole at oral doses up to 150 mg/kg/day (40 times the recommended human dose based on body surface area) was found to have no effect on fertility and reproductive performance of male and female rats.

**Pregnancy: Teratogenic Effects.**

**Pregnancy Category B**

**Lansoprazole**

Teratology studies have been performed in pregnant rats at oral doses up to 150 mg/kg/day (40 times the recommended human dose based on body surface area) and pregnant rabbits at oral doses up to 30 mg/kg/day (16 times the recommended human dose based on body surface area) and have revealed no evidence of impaired fertility or harm to the fetus due to lansoprazole.

There are, however, no adequate or well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Pregnancy Category C**

**Clarithromycin**

See WARNINGS (above) and full prescribing information for clarithromycin before using in pregnant women.

**Nursing Mothers**

Lansoprazole or its metabolites are excreted in the milk of rats. It is not known whether lansoprazole is excreted in human milk. Because many drugs are excreted in human milk, because of the potential for serious adverse reactions in nursing infants from lansoprazole, and because of the potential for tumorigenicity shown for lansoprazole in rat carcinogenicity studies, 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.

**Pediatric Use**

The safety and effectiveness of PREVACID have been established in pediatric patients 1 to 17 years of age for short-term treatment of symptomatic GERD and erosive esophagitis. Use of PREVACID in this population is supported by evidence from adequate and well-controlled studies of PREVACID in adults with additional clinical, pharmacokinetic, and pharmacodynamic studies performed in pediatric patients. The adverse events profile in pediatric patients is similar to that of adults. There were no adverse events reported in U.S. clinical studies that were not previously observed in adults. The safety and effectiveness of PREVACID in patients <1 year of age have not been established.

**1 to 11 years of age**

The pediatric safety of PREVACID Delayed-Release Capsules has been assessed in 66 pediatric patients aged 1 to 11 years of age. Of the 66 patients with GERD 85% (56/66) took PREVACID for 8 weeks and 15% (10/66) took it for 12 weeks.

The most frequently reported (2 or more patients) treatment-related adverse events in patients 1 to 11 years of age (N=66) were constipation (5%) and headache (3%).

**12 to 17 years of age**

The safety of PREVACID Delayed-Release Capsules has been assessed in these 87 adolescent patients. Of the 87 adolescent patients with GERD, 6% (5/87) took PREVACID for <6 weeks, 93% (81/87) for 6-10 weeks, and 1% (1/87) for >10 weeks.

The most frequently reported (at least 3%) treatment-related adverse events in these patients were headache (7%), abdominal pain (5%), nausea (3%) and dizziness (3%). Treatment-related dizziness, reported in this package insert as occurring in <1% of adult patients, was reported in this study by 3 adolescent patients with nonerosive GERD, who had dizziness concurrently with other events (such as migraine, dyspnea, and vomiting).

**Use in Women**

Over 4,000 women were treated with lansoprazole. Ulcer healing rates in females were similar to those in males. The incidence rates of adverse events were also similar to those seen in males.

**Use in Geriatric Patients**

Ulcer healing rates in elderly patients are similar to those in a younger age group. The

incidence rates of adverse events and laboratory test abnormalities are also similar to those seen in younger patients. For elderly patients, dosage and administration of lansoprazole need not be altered for a particular indication.

**ADVERSE REACTIONS**

**Clinical**

Worldwide, over 10,000 patients have been treated with lansoprazole in Phase 2-3 clinical trials involving various dosages and durations of treatment. The adverse reaction profiles for PREVACID Delayed-Release Capsules and PREVACID For Delayed-Release Oral Suspension are similar. In general, lansoprazole treatment has been well-tolerated in both short-term and long-term trials.

The following adverse events were reported by the treating physician to have a possible or probable relationship to drug in 1% or more of PREVACID-treated patients and occurred at a greater rate in PREVACID-treated patients than placebo-treated patients:

**Incidence of Possibly or Probably Treatment-Related Adverse Events in Short-Term, Placebo-Controlled Studies**

Body System/Adverse Event	PREVACID (N= 2768) %	Placebo (N= 1023) %
Body as a Whole		
Abdominal Pain	2.1	1.2
Digestive System		
Constipation	1.0	0.4
Diarrhea	3.8	2.3
Nausea	1.3	1.2

Headache was also seen at greater than 1% incidence but was more common on placebo. The incidence of diarrhea was similar between patients who received placebo and patients who received lansoprazole 15 mg and 30 mg, but higher in the patients who received lansoprazole 60 mg (2.9%, 1.4%, 4.2%, and 7.4%, respectively).

The most commonly reported possibly or probably treatment-related adverse event during maintenance therapy was diarrhea.

In the risk reduction study of PREVACID for NSAID-associated gastric ulcers, the incidence of diarrhea for patients treated with PREVACID was 5%, misoprostol 22%, and placebo 3%. Additional adverse experiences occurring in 1% of patients or subjects in domestic trials are shown below. Refer to **Postmarketing** for adverse reactions occurring since the drug was marketed.

**Body as a Whole** – abdomen enlarged, allergic reaction, asthenia, back pain, candidiasis, carcinoma, chest pain (not otherwise specified), chills, edema, fever, flu syndrome, halitosis, infection (not otherwise specified), malaise, neck pain, neck rigidity, pain, pelvic pain; **Cardiovascular System** – angina, arrhythmia, bradycardia, cerebrovascular accident/cerebral infarction, hypertension/hypotension, migraine, myocardial infarction, palpitations, shock (circulatory failure), syncope, tachycardia, vasodilation; **Digestive System** – abnormal stools, anorexia, bezoar, cardiospasm, cholelithiasis, colitis, dry mouth, dyspepsia, dysphagia, enteritis, eructation, esophageal stenosis, esophageal ulcer, esophagitis, fecal discoloration, flatulence, gastric nodules/fundic gland polyps, gastritis, gastroenteritis, gastrointestinal anomaly, gastrointestinal disorder, gastrointestinal hemorrhage, glossitis, gum hemorrhage, hematemesis, increased appetite, increased salivation, melena, mouth ulceration, nausea and vomiting, nausea and vomiting and diarrhea, oral moniliasis, rectal disorder, rectal hemorrhage, stomatitis, tenesmus, thirst, tongue disorder, ulcerative colitis, ulcerative stomatitis; **Endocrine System** – diabetes mellitus, goiter, hypothyroidism; **Hemic and Lymphatic System** – anemia, hemolysis, lymphadenopathy; **Metabolic and Nutritional Disorders** – gout, dehydration, hyperglycemia/hypoglycemia, peripheral edema, weight gain/loss; **Musculoskeletal System** – arthralgia, arthritis, bone disorder, joint disorder, leg cramps, musculoskeletal pain, myalgia, myasthenia, synovitis; **Nervous System** – abnormal dreams, agitation, amnesia, anxiety, apathy, confusion, convulsion, depersonalization, depression, diplopia, dizziness, emotional lability, hallucinations, hemiplegia, hostility aggravated, hyperkinesia, hypertension, hyposthesia, insomnia, libido decreased/increased, nervousness, neurosis, paresthesia, sleep disorder, somnolence, thinking abnormality, tremor, vertigo; **Respiratory System** – asthma, bronchitis, cough increased, dyspnea, epistaxis, hemoptysis, hiccup, laryngeal edema, pharyngitis, pleural disorder, pneumonia, respiratory disorder, upper respiratory inflammation/infection, rhinitis, sinusitis, stridor; **Skin and Appendages** – acne, alopecia, contact dermatitis, dry skin, fixed eruption, hair disorders, maculopapular rash, nail disorder, pruritus, rash, skin carcinoma, skin disorder, sweating, urticaria; **Special Senses** – abnormal vision, blurred vision, conjunctivitis, deafness, dry eyes, ear disorder, eye pain, otitis media, parosmia, photophobia, retinal degeneration, taste loss, taste perversion, tinnitus, visual field defect; **Urogenital System** – abnormal menses, breast enlargement, breast pain, breast tenderness, dysmenorrhea, dysuria, gynecomastia, impotence, kidney calculus, kidney pain, leukorrhea, menorrhagia, menstrual disorder, polyuria, testis disorder, urinary calculus, urinary tract infection, urinary tract infection, urinary urgency, urination impaired, vaginitis.

**Postmarketing**

On-going Safety Surveillance: Additional adverse experiences have been reported since lansoprazole has been marketed. The majority of these cases are foreign-sourced and a relationship to lansoprazole has not been established. Because these events were reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events are listed below by COSTART body system.

**Body as a Whole** – anaphylactoid-like reaction; **Digestive System** – hepatotoxicity, pancreatitis, vomiting; **Hemic and Lymphatic System** – agranulocytosis, aplastic anemia, hemolytic anemia, leukopenia, neutropenia, pancytopenia, thrombocytopenia, and thrombotic thrombocytopenic purpura; **Skin and Appendages** – severe dermatologic reactions including erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (some fatal); **Special Senses** – speech disorder; **Urogenital System** – urinary retention.

**Combination Therapy with Amoxicillin and Clarithromycin**

In clinical trials using combination therapy with PREVACID plus amoxicillin and clarithromycin, and PREVACID plus amoxicillin, no adverse reactions peculiar to these drug combinations were observed. Adverse reactions that have occurred have been limited to those that had been previously reported with PREVACID, amoxicillin, or clarithromycin.

Triple Therapy: PREVACID/amoxicillin/clarithromycin

The most frequently reported adverse events for patients who received triple therapy for 14 days were diarrhea (7%), headache (6%), and taste perv

# TNF-Blockers Restore Normal Growth in Children

BY ELIZABETH MECHCATIE  
Senior Writer

A study that evaluated children with severe juvenile idiopathic arthritis before and after starting anti-tumor necrosis factor treatment indicated that these biological agents appear to be effective in restoring normal growth in this population, reported Dr. Pirjo Tynjälä.

The results also suggest that the improvements in growth are related to the impact these treatments have on inflammation, wrote Dr. Tynjälä of the Hospital for Children and Adolescents, Helsinki University Central Hospital, and her associates (*Ann. Rheum. Dis.* 2006;65:1044-9).

The study followed the growth of 71 chil-

*Continued from previous page*

gans, longer life expectancy, and more rapid cell division.

Dr. Slovis said that children receive more radiation than do adults when the same dose of radiation is used. Radiation doses are measured with a phantom and set at a fixed midpoint, he said. This measurement is based on 14 slices, but is independent of the thickness of those slices.

Studies of the effects of radiation in the survivors of the atomic bombings of Hiroshima and Nagasaki include data specific to children.

Among the findings noted by Dr. Friedman is an increased incidence of leukemia, breast cancer, colon cancer, thyroid cancer, and lung cancer. These do not occur immediately, but at the times that would be expected for the specific cancer to develop.

Girls are more radiosensitive than boys, he said, and the risk of cancer development varies dramatically with the patient's age at exposure.

Dr. Slovis said some children with hereditary diseases—including ataxia-telangiectasia, basal cell nevus syndrome, Cockayne's syndrome, Down syndrome, Fanconi's anemia, Gardner's syndrome, Nijmegen breakage syndrome, and Usher's syndrome—are extremely sensitive to radiation and should not be exposed at all, if possible.

He also discouraged the use of radiation in children with hereditary syndromes that have been associated with childhood cancers.

Fetuses and premature babies are especially vulnerable, added Dr. Slovis. He hailed the late Dr. Alice Stewart's work for establishing that radiation in utero increases the relative risk of leukemia and other malignancies.

"How much radiation does a 25-week surviving preemie get?" he asked, comparing them to third-trimester fetuses and urging limited testing in infants. "I don't say don't get an indicated CT," he said. "I say get the indications, and work it through." Physicians should be sure each test they order is necessary, should use "the least invasive modality that gives a high certainty of success," and should discuss the case with a pediatric radiologist whenever they are unsure. ■

dren with polyarticular disease—course juvenile idiopathic arthritis for 2 years before and 2 years after starting etanercept (43 patients) or infliximab (28 patients). When treatment started, mean age was 9.6 years, mean disease duration was 5.7 years, and the children were refractory to conventional disease-modifying antirheumatic drugs. The dose of etanercept (Enbrel) was 0.4 mg/kg twice a week; the dose of infliximab (Remicade) was 80-200 mg every 6-8 weeks administered intravenously.

In the group overall, the mean growth velocity increased significantly during treatment, which was mostly because of the increase in the 53 children whose growth was delayed before starting treatment. Among the 18 children whose growth was normal or accelerated before treatment, growth velocity increased, but not significantly, during treatment. Over the 4 years, there were no significant differences in the total steroid dose among those with delayed growth and those with normal growth.

After 24 months of treatment, disease was inactive in 52% of the patients, and activity had decreased in the remainder, Dr. Tynjälä and her colleagues wrote.

The change in inflammatory activity "remained a significant predictor of the growth velocity, even after glucocorticoids were taken into account," suggesting that the improved growth velocity may be because of the reduction in inflammation and not "a direct effect of biological agents on growth or on skeletal maturation." ■

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**OPANA**<sup>®</sup>  
(oxymorphone HCl) 

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**OPANA**<sup>®</sup> **ER**  
(oxymorphone HCl) 

### Extended-release tablets

**OPANA**<sup>®</sup> ER is indicated for the relief of moderate to severe pain in patients requiring continuous, around-the-clock opioid therapy for an extended period of time.

- **OPANA**<sup>®</sup> ER is not intended for use as a prn analgesic.
- **OPANA**<sup>®</sup> ER is not indicated for pain in the immediate postoperative period (12–24 hours following surgery) for patients not previously taking opioids because of the risk of oversedation and respiratory depression requiring reversal with opioid antagonists.
- **OPANA**<sup>®</sup> ER is not indicated for pain in the postoperative period if the pain is mild or not expected to persist for an extended period of time.

### Important Safety Information

**OPANA**<sup>®</sup> and **OPANA**<sup>®</sup> ER are opioid agonists and Schedule II controlled substances with an abuse liability similar to morphine. **OPANA**<sup>®</sup> and **OPANA**<sup>®</sup> ER can be abused in a manner similar to other opioid agonists, legal or illicit.

**OPANA**<sup>®</sup> ER has a boxed warning as follows:

**WARNING: OPANA**<sup>®</sup> ER contains oxymorphone, which is a morphine-like opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics.

Oxymorphone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing **OPANA**<sup>®</sup> ER in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

**OPANA**<sup>®</sup> ER is an extended-release oral formulation of oxymorphone indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.

**OPANA**<sup>®</sup> ER is NOT intended for use as a prn analgesic.

**OPANA**<sup>®</sup> ER TABLETS are to be swallowed whole and are not to be broken, chewed, dissolved, or crushed. Taking broken, chewed, dissolved, or crushed **OPANA**<sup>®</sup> ER TABLETS leads to rapid release and absorption of a potentially fatal dose of oxymorphone.

**Patients must not consume alcoholic beverages, or prescription or nonprescription medications containing alcohol, while on OPANA**<sup>®</sup> ER therapy. The co-ingestion of alcohol with **OPANA**<sup>®</sup> ER may result in increased plasma levels and a potentially fatal overdose of oxymorphone.

**OPANA**<sup>®</sup> and **OPANA**<sup>®</sup> ER are **contraindicated** in patients with a known hypersensitivity to oxymorphone hydrochloride, morphine analogs such as codeine, or any of the other ingredients of **OPANA**<sup>®</sup> and **OPANA**<sup>®</sup> ER; in patients with moderate or severe hepatic impairment or in any situation where opioids are contraindicated such as: patients with respiratory depression (in the absence of resuscitative equipment or in unmonitored settings), acute or severe bronchial asthma, hypercarbia, and in any patient who has or is suspected of having paralytic ileus.

Respiratory depression is the chief hazard of **OPANA**<sup>®</sup> and **OPANA**<sup>®</sup> ER, particularly in elderly or debilitated patients. **OPANA**<sup>®</sup> and **OPANA**<sup>®</sup> ER should be administered with extreme caution to patients with conditions accompanied by hypoxia, hypercapnia, or decreased respiratory reserve such as: asthma, chronic obstructive pulmonary disease or cor pulmonale, severe obesity, sleep apnea syndrome, myxedema, kyphoscoliosis, central nervous system (CNS) depression, or coma.

Patients receiving other opioid analgesics, general anesthetics, phenothiazines or other tranquilizers, sedatives, hypnotics, or other CNS depressants (including alcohol) may experience additive effects resulting in respiratory depression, hypotension, profound sedation, or coma. **OPANA**<sup>®</sup> and **OPANA**<sup>®</sup> ER should be used with caution in elderly and debilitated patients and in patients who are known to be sensitive to CNS depressants, such as those with cardiovascular, pulmonary, renal, or hepatic disease. **OPANA**<sup>®</sup> and **OPANA**<sup>®</sup> ER should be used with caution in patients with mild hepatic impairment and in patients with moderate to severe renal impairment. These patients should be started cautiously with lower doses of **OPANA**<sup>®</sup> or **OPANA**<sup>®</sup> ER while carefully monitoring for side effects.

**OPANA**<sup>®</sup> ER is not indicated for preemptive analgesia (administration preoperatively for the management of postoperative pain).

The most common adverse drug reactions (≥10%) reported at least once by patients treated with **OPANA**<sup>®</sup> in all clinical trials were nausea and pyrexia. The most common adverse drug reactions (≥10%) in all clinical trials for **OPANA**<sup>®</sup> ER were nausea, constipation, dizziness (excluding vertigo), vomiting, pruritus, somnolence, headache, increased sweating, and sedation.

**Please see accompanying Brief Summaries of full Prescribing Information, including boxed warning on OPANA**<sup>®</sup> ER, on the following pages.