

Top 5 Skin Diagnoses Vary by Ethnicity in Study

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MIAMI — Unique structural and functional differences between the skin of black and white patients might help explain differences in the top five dermatology diagnoses for each ethnicity, according to study data presented at an international symposium sponsored by L'Oreal Institute for Ethnic Hair and Skin Research.

Prior to this study, the most recent sur-

vey of cutaneous diseases in black Americans was published more than 2 decades ago (*Cutis* 1983;32:388-90), said Dr. Amanda B. Sergay, a third-year dermatology resident at St. Luke's-Roosevelt Hospital Center in New York City.

Dr. Sergay and her associates, including principal investigator Dr. Andrew F. Alexis, retrospectively compared the diagnostic codes for 1,074 black and white patient visits treated at the Skin of Color Center at St. Luke's-Roosevelt Hospital Center,

New York City, from August 2004 to July 2005. When ethnicity was unclear, the patient's own description was used.

Acne vulgaris was the most common diagnosis in both groups (ICD-9 code 706.1). "The pathophysiology of acne is not thought to differ between races or ethnicities," she said at the symposium, which was also sponsored by Howard University.

Acne and dyschromia (code 709.09) are so common that they accounted for almost 50% of black patient visits (*Cutis*, in

press: November 2007). Black patients also were commonly diagnosed with contact dermatitis and other eczema, unspecified cause (code 692.9), alopecia (code 704.0), and seborrheic dermatitis (code 690.1).

After acne vulgaris, the most common diagnoses in white patients were a lesion of unspecified behavior (code 238.2), benign neoplasm of the skin of the trunk (code 216.5), contact dermatitis or other eczema, and psoriasis (696.1).

In black patients, dyschromia and alope-

Amitiza®

(lubiprostone) Capsules

Initial U.S. Approval: 2006

BRIEF SUMMARY OF PRESCRIBING INFORMATION- Please see package insert for complete prescribing information.

1 INDICATIONS AND USAGE

Amitiza® is indicated for the treatment of chronic idiopathic constipation in adults.

2 DOSAGE AND ADMINISTRATION

The recommended dosage for Amitiza is 24 mcg taken twice daily orally with food. Physicians and patients should periodically assess the need for continued therapy.

3 DOSAGE FORMS AND STRENGTHS

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

4 CONTRAINDICATIONS

Amitiza is contraindicated in patients with known mechanical gastrointestinal obstruction.

5 WARNINGS AND PRECAUTIONS

5.1 Pregnancy

The safety of Amitiza in pregnancy has not been evaluated in humans. In guinea pigs, lubiprostone has been shown to have the potential to cause fetal loss. Amitiza should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Women who could become pregnant should have a negative pregnancy test prior to beginning therapy with Amitiza and should be capable of complying with effective contraceptive measures. See *Use in Specific Populations* (8.1).

5.2 Nausea

Patients taking Amitiza may experience nausea. If this occurs, concomitant administration of food with Amitiza may reduce symptoms of nausea. See *Adverse Reactions* (6.1).

5.3 Diarrhea

Amitiza should not be prescribed to patients that have severe diarrhea. Patients should be aware of the possible occurrence of diarrhea during treatment. Patients should be instructed to inform their physician if severe diarrhea occurs. See *Adverse Reactions* (6.1).

5.4 Bowel Obstruction

In patients with symptoms suggestive of mechanical gastrointestinal obstruction, the treating physician should perform a thorough evaluation to confirm the absence of such an obstruction prior to initiating therapy with Amitiza.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Adverse reactions in dose-finding, efficacy, and long-term clinical studies:

The data described below reflect exposure to Amitiza in 1175 patients (29 at 24 mcg once daily, 1113 at 24 mcg twice daily, and 33 at 24 mcg three times daily) over 3- or 4-week, 6-month, and 12-month treatment periods; and from 316 patients receiving placebo over short-term exposure (≤ 4 weeks). The total population (N = 1491) had a mean age of 49.7 (range 19–86) years; was 87.1% female; 84.8% Caucasian, 8.5% African American, 5.0% Hispanic, 0.9% Asian; and 15.5% elderly (≥ 65 years of age). Table 1 presents data for the adverse reactions that occurred in at least 1% of patients who received Amitiza (any dosage) and that occurred more frequently with study drug than placebo. In addition, corresponding adverse reaction incidence rates in patients receiving Amitiza 24 mcg once daily and in patients receiving Amitiza 24 mcg twice daily are shown.

Table 1: Percent of Patients with Adverse Reactions in Clinical Studies of Amitiza

System/Adverse Reaction ¹	Placebo	Amitiza	Amitiza	Amitiza
	N = 316 %	24 mcg Once Daily N = 29 %	24 mcg Twice Daily N = 1113 %	Any Dosage ² N = 1175 %
Gastrointestinal disorders				
Nausea	3	17	29	29
Diarrhea	<1	7	12	12
Abdominal pain	3	3	8	8
Abdominal distension	2	–	6	6
Flatulence	2	3	6	5
Vomiting	–	–	3	3
Loose stools	–	–	3	3
Abdominal discomfort ³	–	3	2	2
Dyspepsia	<1	–	2	2
Dry mouth	<1	–	1	1
Stomach discomfort	<1	–	1	1
Nervous system disorders				
Headache	5	3	11	11
Dizziness	<1	3	3	3
General disorders and site administration conditions				
Edema	<1	–	3	3
Fatigue	<1	–	2	2
Chest discomfort/pain	–	3	2	2
Respiratory, thoracic, and mediastinal disorders				
Dyspnea	–	3	2	2

¹ Includes only those events associated with treatment (possibly, probably, or definitely related, as assessed by the investigator).

² Includes patients dosed at 24 mcg once daily, 24 mcg twice daily, and 24 mcg three times daily.

³ This term combines "abdominal tenderness," "abdominal rigidity," "gastrointestinal discomfort," and "abdominal discomfort."

Nausea: Approximately 29% of patients who received Amitiza (any dosage) experienced an adverse reaction of nausea; 3% of patients had severe nausea while 8% of patients discontinued treatment due to nausea. The rate of nausea associated with Amitiza (any dosage) was substantially lower among male (7%) and elderly patients (18%). Further analysis of the safety data revealed that long-term exposure to Amitiza does not appear to place patients at an elevated risk for experiencing nausea. The incidence of nausea increased in a dose-dependent manner with the lowest overall incidence for nausea reported at the 24 mcg once daily dosage (17%). In open-labeled, long-term studies, patients were allowed to adjust the dosage of Amitiza down to 24 mcg once daily from 24 mcg twice daily if experiencing nausea. Nausea decreased when Amitiza was administered with food. No patients in the clinical studies were hospitalized due to nausea.

Diarrhea: Approximately 12% of patients who received Amitiza (any dosage) experienced an adverse reaction of diarrhea; 3% of patients had severe diarrhea while 2% of patients discontinued treatment due to diarrhea.

Electrolytes: No serious adverse reactions of electrolyte imbalance were reported in clinical studies, and no clinically significant changes were seen in serum electrolyte levels in patients receiving Amitiza.

Less common adverse reactions: The following list of adverse reactions includes those that occurred in less than 1% of patients receiving Amitiza (any dosage) in dose-finding, efficacy, and long-term clinical studies and that were considered by the investigator to be probably or definitely related to treatment with study drug. Moreover, the list includes only those events that occurred in at least two patients and more frequently in patients receiving Amitiza than those receiving placebo.

Gastrointestinal disorders: fecal incontinence, defecation urgency, frequent bowel movements, intestinal functional disorder, constipation, eructation
Musculoskeletal and connective tissue disorders: muscle cramp, joint swelling, myalgia

Nervous system disorders: dysgeusia, syncope, tremor

Respiratory, thoracic, and mediastinal disorders: pharyngolaryngeal pain, cough

Skin and subcutaneous tissue disorders: hyperhidrosis, cold sweat
General disorders and administration site conditions: influenza, pain

Metabolism and nutrition disorders: decreased appetite

Psychiatric disorders: anxiety

cia made the top-5 list, but they were not among the top 10 diagnoses for white patients, Dr. Sergay said. The dyschromia diagnoses included postinflammatory hyperpigmentation and melasma.

"Postinflammatory hyperpigmentation is a common sequela of cutaneous injury or irritation in skin of color," Dr. Sergay said. It can also result from pseudofolliculitis barbae, which is more common in black than in white patients because of structural differences in the hair follicle and shaft.

The higher incidence of alopecia in black patients could be partially explained by the fact that there are fewer elastic fibers in black skin to anchor hair follicles to the der-

mis (Dermatol. Clin. 1988;6:271-81). Chemical and physical hair care practices may also contribute to alopecia, as could the significantly lower total hair density and number of hair follicles in black patients, compared with whites (Dermatol. Clin. 2003;21:595-600; Arch. Dermatol. 1999;135:656-8).

Racial variations in skin physiology may also lead to differences in eczema prevalence, Dr. Sergay said.

The single-center source of information was a limitation of the study, as was potential selection bias from participating physicians, she said, adding that categorization of patient ethnicity by a physician or assistant is less reliable than self-reporting. ■



Melasma, a skin pigmentation disorder, manifests as dark spots on the face.



Blacks' skin physiology and hair-care practices make them prone to alopecia.

PHOTOS COURTESY DR. PEARL E. GRIMES

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:

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and

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Few Seek Medical Advice for Problems Linked to Hair Care

MIAMI — Many black women experience adverse events and dissatisfaction stemming from their hair care practices, but few seek medical advice, results of a survey presented at an international symposium sponsored by L'Oréal Institute for Ethnic Hair and Skin Research indicate.

"A few years ago, I noticed scalp and hair conditions were a common complaint among black women in my practice," said Dr. Maria C. Rios, a clinical dermatologist in Montevideo, Uruguay. Physicians "need to recognize scalp and hair conditions associated with some procedures used by this ethnic group."

All 42 adult women (aged 18-60 years) surveyed used chemical or physical hair straightening techniques. Hair and scalp disorders occurred in 70% of respondents.

Following a physical examination and clinical photography, each woman completed a brief questionnaire, noting how satisfied they were with the ethnic or natural aspect of their hair, hair care practices, and any clinical presentations related to hairstyle management. The majority, 37 women, reported dissatisfaction with the ethnic aspect of their hair. A total of 26 reported a history of dermatologic lesions or other scalp/hair conditions.

Twenty women experienced irritant contact dermatitis after use of a chemical relaxer. Nine used a commercial brand and 11 used a product with "banana extract." Although participants reported great hair straightening results with banana extract, all who used it experienced stinging, burning, itchiness, flaking, and/or pain, Dr. Rios said at the meeting, which was also sponsored by Howard University.

Seven women reported scarring alopecia; five attributed the condition to chemical use, one to thermal hair treatment, and another to both practices. Three participants reported nonscarring alopecia related to their hair care.

One of the 26 women experienced allergic dermatitis after use of a chemical relaxer and hair dye at almost the same time, Dr. Rios said. A total of six women experienced burns, four from chemicals and two from hair ironing. A total of 16 women reported temporary hair loss and breakage. Interestingly, only four of these women sought medical advice.

—Damian McNamara