ACG 2007 an Overwhelming Success

More than 4,000 attendees converged on Philadelphia for ACG 2007, making it the second highest attended ACG meeting ever. From the Friday courses to the Postgraduate Course and the Annual Meeting, the educational agenda was top-notch and provided the latest clinical updates.

A few of the many highlights from the meeting included:

- Negotiation expert, Roger Dawson, offering Practice Management Course attendees a lesson on negotiating and how to become a power negotiator.
- New format for the Postgraduate Course Learning Luncheons which focused on “How I Do It” for Saturday luncheons and “You Make the Call” for Sunday luncheons.
- The GI Jeopardy competition with the winning team from Mayo School of Graduate Medical Education (Rochester) earning the GI Cup for 2007.
- The first annual ACG Allied Health Professionals Symposium, designed specifically for allied health personnel, explored the topic of A Case Based Approach to the Management of GI Diseases.
- The American Journal of Gastroenterology Lecture, “NOTES: Just Because We Can, Should We?” which featured leading experts Anthony Kalloo, MD, FACC and Jeffrey Ponsky, MD, FACC taking point/counterpoint views on the subject.

Many of the educational sessions from the meeting will be available to view online at the ACG Education Universe in the coming months. For those who did not pick up their CME certificate on-site, you may print your certificate online by visiting www.acg.gi.org.

Look for additional ACG 2007 highlights in the December issue of the ACG Update.

Best Practices 2008 Agenda Slated

Popular Governors’ course moves to new location in Palm Springs/Indian Wells, California

Every two years, the ACG Board of Governors, in conjunction with the ASGE, offers a 2½ day course highlighting the latest clinical updates. The program features ACG leaders, including current and past ACG Governors, and ASGE leaders as faculty. These are well-known, national experts who will provide the latest clinical updates and tips on how to incorporate them into patient care. The 2008 course moves to a new location, the Hyatt Grand Champions in Indian Wells, California, just minutes from Palm Springs. It’s a great time of the year to escape the winter cold you may be experiencing to enjoy golf, tennis, warm days, cool nights and relaxation.

The program kicks off on Friday, February 1, with an optional course on sedation, “Current Issues and Controversies in Endoscopic...”
FROM THE PRESIDENT

Working Towards a Better Outcome for Clinical Gastroenterology

By Amy E. Foxx-Orenstein, DO, FACG

As I embark on my year as ACG President, I am humbled and honored to serve you. Serving as the second woman to hold the position of College president, I look back and appreciate what the election of the first female president, Past President Christina Surawicz, MD, FACG, meant to me personally and what her leadership brought to the College. I hope that my unique perspective on leadership will help inspire other women who continue to enter the specialty in even greater numbers.

Since the last issue of the ACG Update, the College held its Annual Scientific Meeting and Postgraduate Course. The meeting was very successful with more than 4,000 attendees, the second largest attendance ever for an ACG meeting. The educational program was exceptional and a variety of networking events provided attendees the opportunity to connect with old colleagues and make new contacts. You’ll find several highlights about the meeting in this issue as well as in the upcoming December issue. If you have never been to the ACG Annual Scientific Meeting and Postgraduate Course, I encourage you to do so next year. ACG returns to the beautiful Gaylord Palms Resort & Convention Center in Orlando, Florida, October 3-8, 2008. Find out more about what to do and see while in Orlando on page 6.

One major highlight of the 2007 meeting was the celebration of ACG’s 75th Anniversary. In honor of our 75th Anniversary, ACG produced a book, “American College of Gastroenterology, 1932-2007, 75 Years of Commitment to Clinical Gastroenterology, Gastroenterologists, and Patient Health.” Initiated by the Archives Committee, the book chronicles ACG’s 75 years. The Archives Committee, as well as many past and present leaders of the College, worked tirelessly in producing a wonderful remembrance of the first 75 years. Learn more about the book on page 4. We’ll highlight additional efforts for the 75th anniversary in the December issue of the ACG Update.

As I look to the year ahead and what will impact practice, decisions by policymakers will continue to challenge the practice of gastroenterology. You’ve likely read a significant amount of news from the College these past months regarding plans for ASC payment cuts, cuts to core GI services, and overall downward pressure on physician reimbursement under the current system. Many members have taken time out of their busy practice to educate lawmakers and regulators about these important issues through meetings, by filing comments and sending letters. 2008 will provide us another opportunity for the College to educate and assist our members as well as the policymakers that have produced these misguided policies as we attempt to obtain a better outcome for clinical gastroenterology.

Having served as National Affairs Committee chair for three years, Dr. Edward Cattau’s tenure comes to an end. We have the luxury of having Scott Tenner, MD, MPH, FACG, a savvy and experienced participant in National Affairs activities through his participation in the Committee as well as an ACG Governor, to assume the committee chair so that the College will not miss a beat. If you have not reached out to your leaders in Congress to share your views on these important issues, we encourage you to do so. Included in this issue of the Update is the latest information on policy issues, or see President’s Message, page 7
ACG Takes Deliberative, Evidence-Based Approach to Coding for CT Colonography

The College continues in its efforts to secure access to new diagnostic and screening technologies colorectal cancer for the membership. As with each advance in technology, the College has made the case to public policymakers and insurance carriers that the quality of the scientific evidence should drive reimbursement decisions. Securing an appropriate role for those clinical gastroenterologists who choose to adopt or embrace particular technologies is paramount. The latest technology making its way through this evaluation process is CT colonography. While there are indications that sensitivity of this test for identifying polyps greater than 6 mm is advancing when done with the appropriate equipment and software, the pivotal study has not yet been fully presented nor has it been accepted for publication. Once there is peer reviewed acceptance/publication in a peer reviewed journal, the data can be used for evaluating whether a Category 1 CPT code that will permit payment under Medicare will be available for use by the CPT Editorial Panel. As this technology advances, the College will continue to fight for a coding structure that distinguishes between screening and diagnostic procedures as is the case with optical colonoscopy under Medicare. Furthermore, a split code that permits separate billing codes for intra-luminal reads and extra-luminal reads will be important as well to try to both facilitate a more rational reimbursement model and protect against unnecessary liability from extra-colonic imaging.

In the view of the College, there continues to be several very important issues that need to be resolved before CT colonography is accepted as another tool for gastroenterologists and others in the fight against colorectal cancer. Specifically, there continue to be unanswered questions regarding how polyps less than 6 mm in diameter will be treated. Some in the radiology community have suggested that these polyps simply go unreported. ACG finds this approach unacceptable and believes any lesions identified, no matter how small, must be reported. There is also a need to determine appropriate surveillance intervals for CT colonography based on sound evidence. This data does not appear to exist at this time. Furthermore, important questions remain regarding radiation exposure risks to patients with repetitive exposures, in particular, those who are obese. In addition to these key scientific issues, there are also crucial questions about the economic impact of this technology on the healthcare system.

The ACG, along with other interested parties, has been involved in a CPT workgroup process that was created by the CPT Editorial Panel to deal with the significant issues associated with CT colonography in the Medicare system which then drives decisions among the private payers. The College remains committed to participating in the CPT workgroup process so these issues can be fully discussed and appropriately resolved to promote and insure that the clinical gastroenterologist has adequate input into these decisions. The ACG goals are twofold: (1) to assure that the appropriate rules of evidence and science are used to guide these decisions, and (2) to develop strategies that effect the best outcomes for patients who undergo these procedures for either diagnostic or screening examinations. We firmly believe that the GI/Radiology workgroup suggested by the AMA is where this issue should be addressed.

Notwithstanding the creation of the special workgroup by the CPT Editorial Panel, applications for a Category 1 Code were filed before the deadline for applications to be considered at the February 2008 CPT meeting, one by the AGA and one by the American College of Radiology (ACR). Both organizations have been participating in the workgroup process and ACG was disappointed to see the process bypassed with the filing of these applications. At the time of this writing, it was still unclear whether CPT would refer this matter back to the work group, as ACG and ASGE have suggested, or whether it will now proceed through the standard CPT code process.

How the CPT Code Assignment Process Works
For the AMA Editorial Panel to grant a Category 1 Code, the following criteria have to be met:

- The procedure must be FDA approved;
- The procedure must be performed across the country in multiple locations;
- Many people must perform the procedure; and
- The clinical efficacy of the procedure must be well-established through studies published in the peer-reviewed literature.

While it is likely that CT colonography meets the first three criteria, the key study known as the ACRIN trial has not yet been accepted for publication in a peer reviewed journal. While it is quite possible that this will occur before the CPT meeting in February, if it does not, the College maintains that the last criterion would not be met. If it is published and can be reviewed, the College is prepared to do so and participate in the CPT review process.

Dangers from Premature Adoption?
The ACG believes that there is a risk associated with any technology such as CT colonography being prematurely granted. A Category 1 CPT code could expedite the technology’s adoption by inadequately trained personnel or persons using out-of-date equipment or perhaps lead to the non-reporting of small lesions. Furthermore, there is a significant risk of giving patients a false sense of security about their colorectal cancer or polyp status if the implementation and use of the technology is not handled properly.

ACG does not know to what extent clinical gastroenterologists will want to...
New Findings Presented at ACG 2007 Meeting
Generate Media Coverage

New scientific research presented at the ACG Annual Scientific Meeting in Philadelphia gained extensive media pick-up, including numerous media hits from newswire services, the Internet media, newspapers, as well as some television coverage.

ACG presented 11 press releases, each drawing attention to important and newsworthy scientific findings in the field of digestive diseases. Among the research highlighted in ACG’s media outreach: Post-Op Nutrient Deficiencies Associated with Gastric Bypass Surgery; Nocturnal GERD, Sleep Issues and Quality of Life; Functional GI Disorders Impact Productivity Equal to One Lost Day of Work Per Week; and First Colonoscopy with Removal of Polyps Linked to Reduction in Colon Cancer Death.

While many of the findings gained media attention, the “news you can use” approach highlighting lifestyle-oriented themes and quality of life issues generated high interest among the consumer health press.

One particular study that gained extensive media coverage was by Dr. Joseph C. Anderson and Stony Brook University, which found obesity to be the strongest risk factor for colorectal cancer in women, an even stronger association than smoking. Another study generating media interest linked nighttime acid reflux, and other less typical symptoms of GERD, to significant sleep problems.

There was high interest from reporters in results of a study by Dr. David A. Johnson and his colleagues at Eastern Virginia Medical School that revealed an alarming instance of patients underreporting their use of NSAIDs to their doctors. The results of this study aired on CNN, and were featured in several major newspapers including Forbes and U.S. News and World Report.

ACG received several media “hits” from television stations across the country, including major cities such as Chicago, Philadelphia, Denver, and Albuquerque, according to a report gathered by Video Monitoring Services of America. These scientific findings profiled by the College also gained media pick-up from the Internet media and several newswires including UPI, Reuters, WebMD, DocGuide, Science Daily, Health Day, and Medpage Today.

ACG’s “Prescription for Success: Careers in Medicine” program was also a media outreach success. The program, which inspires high school students to consider a career in the medical field, aired on two Philadelphia television stations, WCAU-TV (NBC) and WPVI-TV (ABC), and the Philadelphia Tribune, the nation’s oldest running African-American newspaper, covered the event.

ACG Celebrates 75th Anniversary

Commemorative book marks ACG milestone

ACG marks its 75th Anniversary in 2007 and to celebrate, we’ve published a book that highlights our history. There is a long list of individuals, members past and present, who have contributed to the publication, compiling ACG’s history and various milestones throughout our 75 years. ACG thanks all those individuals who have contributed their time to see this book come to fruition.

In addition, the Archives Committee has put so much of their time into developing this book as well and ACG wishes to recognize the ACG Archives Committee members:

Kevin W. Olden, MD, FACG, Chair
James L. Achord, MD, MACG
V. Alin Botoman, MD, FACG
Mitchell S. Cappell, MD, FACG
Robert E. Kravetz, MD, MACG
Myron Lewis, MD, MACG
Arvey I. Rogers, MD, MACG
Sidney Winawer, MD, MACG
Alvin Zfass, MD, MACG

Committee members want to personally recognize the late Albert C. Svoboda, MD, MACG, who, prior to his passing, dedicated a great deal of time to this project as it came to fruition. A special acknowledgement of Dr. Svoboda is included in the book.
International Perspective was Explored During ACG 2007

ACG's International Relations Committee sponsored special afternoon symposia during Annual Meeting

This article is the first in a series of articles written and submitted by the ACG International Relations Committee on a wide range of topics which will be of interest to all ACG members.

By Christopher Y. Kim, MD, FACG

During the 2007 ACG Annual Scientific Meeting in Philadelphia, the ACG International Relations Committee sponsored its first symposium. With ACG’s outreach expanding to a more international membership, along with gastroenterologists in North America treating an increasingly diverse population, the Committee felt a symposium to address this audience should be organized. The topic chosen was “Screening for GI Malignancies: An International Perspective.”

The symposium focused on the most common gastrointestinal cancers and differences in screening practices for these cancers worldwide. The symposium was moderated by Lewis Roberts, MB, ChB, PhD (Mayo Clinic, Rochester, MN).

The first topic, “Colorectal Cancer: Not Just a Western Disease,” was presented by Massimo Crespi, MD, FACG (National Cancer Institute Regina Elena; Rome, Italy). Dr. Crespi stated that colorectal cancer (CRC) is a deadly but preventable disease that is becoming a problem in developing nations as a consequence of extended life expectancy and adoption of “westernized” lifestyle behaviors. Worldwide, CRC ranks third in incidence and fourth in mortality amongst all cancers (from the 2002 GLOBOCAN report). Developing nations contribute 35% of these figures. Dr. Crespi also pointed out that in Europe, 5-year survival rates for CRC in European countries range from 27-60%, compared with SEER data in the U.S. at 57-65%. The poorer survival in developing nations as well as some European nations is related to the absence of screening and to poor overall performance of the national health systems, partly due to limited resources allocated to health. Screening for CRC in most countries that have programs is by fecal occult blood testing (guaiac or quantitative immunological) every 1 or 2 years. In the European Union countries, only about half of the countries have defined guidelines for CRC. Primary screening colonoscopies (once every 10 years or lifetime) is an option offered by the health services of a few nations in Europe (Austria, Germany, Italy, Luxemburg, Poland) and the U.S. Dr. Crespi concluded by stating that in many developing and even developed countries, CRC screening of any type is hampered by scarce healthcare resources as well as a general cultural gap by health professionals and the public. A key to improving compliance would be in the education of the general practitioner regarding CRC screening and providing financial incentives to increase screening rates.

The second topic was “Esophageal and Gastric Cancer: Are We Doing Any Better?” presented by Hidekazu Suzuki, MD, PhD (Keio University School of Medicine; Tokyo, Japan). Esophageal cancer incidence is on the rise worldwide, and is eighth in incidence and sixth in mortality for all cancers. Adenocarcinoma has supplanted squamous cell carcinoma as the most common type of esophageal cancer in Western countries. However, worldwide, the areas with the highest incidence of esophageal cancers remain in East Asia, Africa, and to a lesser extent in South America, and in these areas, squamous cell carcinoma is still primary. Even though dysphagia, odynophagia and unintentional weight loss are the most common presenting symptoms for esophageal cancer, the incidence is so low not to warrant screening in the general population. The situation is different for gastric cancer, where the incidence is fourth but the mortality is second overall for all cancers, accounting for 700,000 deaths worldwide. The predominant areas are East Asia, Africa, and parts of South America.

Gastric colonization with H. pylori and conditions resulting in chronic atrophic gastritis have been reported as definite risk factors along with causal elements of smoking and diet (e.g., high salt intake and low intake of fruits and vegetables). As in most cancers, the early stages are asymptomatic. In Japan, rigorous screening processes have led to a greater number of gastric cancers being detected at an early stage. Screening for gastric cancer often starts at the age of 40. Screening methods differ depending on resources available, including double contrast barium swallow, EGD, and serum tests for H. pylori, IgG and pepsinogen.

The final topic, “Hepatocellular Carcinoma: A World-Wide Problem,” was presented by Dr. Roberts. Hepatocellular carcinoma (HCC) is sixth in incidence but third in death overall worldwide for all cancers. The highest incidence areas are in Eastern Asia, Southeastern Asia, sub-Saharan Africa, and Southern Europe with the Americas being an area of lowest incidence. Chronic hepatitis B (HBV) infection as well as high-level exposure to dietary aflatoxins lead to Asia and Africa being regions of highest incidence. Screening is possible for HCC in high risk populations, usually with ultrasound every 6 months (with alpha feto-protein reserved for those who are obese leading to poor liver visualization or those without access to high quality liver ultrasounds). Japan, which has aggressive screening and treatment for HCC, has 5-year survival rates over 50%, while in sub-Saharan Africa, without any screening, 5-year survival rates can be as low as 5%. The AASLD published guidelines in 2005 for high-risk HCC individuals. Those individuals include Hepatitis B carriers (Asian males >=40; Asian females >=50; African males >20; carriers with cirrhosis, family history of HCC, and high HBV DNA with ongoing inflammatory activity) and non-HBV cirrhosis patients (Hepatitis C, See International Perspective, page 7
Warm Breezes, Sunshine, Education and Adventure in ‘08!

The ACG Annual Scientific Meeting and Postgraduate Course returns to Orlando, October 3-8, 2008, at the Gaylord Palms Resort & Convention Center. While we can’t guarantee perfect weather, there is a great possibility that you’ll find warm breezes, sunshine, and a great adventure in Orlando. You’ll spend less time traveling to the meeting area from your hotel because the meeting is all under one roof.

When you plan your days away from the office to attend the ACG 2008 meeting, make sure you include in your plans the opportunity to get out and explore Orlando. Regardless of which direction you head, you’ll find adventure along the way. Disney World is just a few miles away from the Gaylord Palms Resort. Bring the kids (regardless of their age) or act like a kid and enjoy the many amusement rides at Disney World. Whether you are a Disney movie fan or not, you can’t help but smile seeing the many movie characters that have made millions of people laugh for decades.

Bonjour! Buon Giorno! Hello! That’s you visiting Epcot and greeting the many international citizens at the various country pavilions. You won’t need your passport when you visit the 11 country pavilions (including the U.S.A.) plus a variety of other pavilions like Imagination Pavilion, Mission: SPACE Pavilion, The Seas with Nemo & Friends Pavilion and more. Other Disney parks include Animal Kingdom, MGM Studios, and two water parks, Blizzard Beach and Typhoon Lagoon.

Ever want to experience all the action you see in your favorite movies or TV show? Make a trip to Universal Studios Florida, the #1 movie and TV based theme park in the world. Some highlights include the Revenge of the Mummy thrill ride, MEN IN BLACK™ Alien Attack™ interactive ride, and OgreVision in Shrek 4-D™. For the truly adventurous, be one of the audience participants in Fear Factor Live.

While Orlando is located in central Florida far from ocean waters, you can still explore the greatest creatures of the sea with a visit to Sea World. Shamu is always a major attraction, but there is so much more to see. Wild Arctic features polar bears, walruses, beluga whales, harbor seals, and trout. The Manatee Reserve gives you the opportunity to see these gentle giants up close. You’ll also see dolphins at the Dolphin Cove and the Dolphin Nursery. During your visit to Sea World, you’ll also encounter sharks, penguins, stingrays, turtles and more. In between the undersea education, have a scream on one of the various rides at the park.

We’ve highlighted several of the theme parks in Orlando, but if the recreation that is calling you involves a club, a ball, some skill and a little patience, you have more than 170 golf courses within an hour distance from Orlando to choose from. Located in Recreation Park at the Gaylord Palms Resort is the Coquina Dunes, presented by Falcon’s Fire Golf Club, which is a 9-hole executive putting course providing all the challenges of a full-size golf course, complete with sand traps, roughs and dogleg bends. If you want to improve your golf game, you can also have some fun at one of the many golf academies in the area.

Ever dream of going into space? Visit Kennedy Space Center Visitor Complex for “Launch Shuttle Experience.” Developed by NASA and its astronauts, feel the rush that the astronauts do every time they take off.

After your many theme park experiences, you can partake in a common recreational activity: shopping! Orlando offers a variety of shopping malls that offer high-end retailers like Neiman Marcus, Saks Fifth Avenue, Nordstrom and more.

We hope you join your colleagues for ACG 2008 in sunny Orlando, Florida. Information about the ACG 2008 educational program will be available in early 2008. Make your vacation plans now by visiting www.orlandoinfo.com.
President’s Message

continued from page 2

you can visit the National Affairs section of the ACG website at www.acg.gi.org for more information.

In addition to the change in committee chair for National Affairs, the Educational Affairs Committee Chair will also be transitioning. Ending her tenure as Educational Affairs Committee Chair is Carol A. Burke, MD, FACP. For three years, Carol has led the committee in developing and implementing the annual scientific meeting program as well as other programs. I want to thank Carol for her significant contribution to the College and for a job well done as Committee Chair. Moving into the Chair position is Jean-Paul Achkar, MD, FACP. Having served on the Committee for several years, he was also one of the Postgraduate Course Directors in 2005 and has overseen development of the Self-Assessment Test for the past three years.

Dr. Achkar is quite knowledgeable in the educational activities of the College and will serve the College well as Educational Affairs Committee Chair for the coming years.

In future issues of the Update, I’ll highlight the many activities of the College’s committees (22 in all) as well as the Board of Governors. I’d also like to take this opportunity to thank all of the College’s committee and Board of Governors members for contributing a significant amount of personal time in support of the College and its programs.

One activity that I will focus on this year is the College’s involvement in the Coalition to End Obesity (CEO). This group grew out of a conference held last May in which the College was the only physician specialty organization involved with a diverse group of other players in healthcare including the American Heart Association, America’s Health Insurance Plans, the Grocery Manufacturers of America and others. The College will be co-chairing the Health System Restructuring Group within the coalition. In light of the enormous impact of obesity on society and the related GI conditions and risks, it is an important opportunity for the College to take a leading role in raising the profile of these issues and to be involved in shaping the policies that will impact our practices in the future.

I mentioned briefly the Annual Meeting which just took place, but the College still has a full educational agenda in the months ahead. In November and December the College offers five more Saturday with GI Experts courses: Los Angeles, California on November 3; Houston, Texas on November 10; Fort Lauderdale, Florida on December 1; Orlando/Kissimmee, Florida on December 8; and Seattle, Washington on December 15. Additional Saturday with GI Experts programming will be offered in 2008. Updates will be posted on the ACG website.

Coming in early 2008 is the ACG Board of Governors/ASGE Best Practices 2008, February 1-3, at the Hyatt Grand Champions Resort & Spa in Indian Wells, California, just outside of Palm Springs. If you are looking for some relaxation after a busy holiday season and want to escape winter’s cold, join your colleagues at this jointly sponsored event. Learn more about this course on page 1.

In closing, I want to thank the many people who have supported me as I assumed the presidency of the College and who will support me throughout the coming year.

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CT Colonography

continued from page 2

integrate this new technology into their practice in light of the effectiveness of other options, unanswered technical and safety questions and the ultimate reimbursement policies. However, once it is clear that the evidence is acceptable for CT colonography, ACG will continue to work to ensure that GIs who wish to do so can perform the intraluminal readings using CT colonography once trained on the new technology. We believe that no one knows the colon better than GIs and the College will fight efforts by the radiologists to prevent GIs from being paid for the professional component of such readings. While the College is committed to embracing well founded, scientifically sound technological advances in colorectal cancer screening and diagnostics, ACG does not want to take any steps that would prematurely advance a technology that is not ready for widespread use or that is in any way restricted from use by appropriately trained gastroenterologists.

Ad Hoc Panel on CTC

ACG is pleased that it is part of an ad hoc AMA CPT Editorial workgroup on CT colonography established by the leadership of the CPT Editorial Panel. R. Bruce Cameron, FACP, ACG’s current CPT Editorial Panel Advisor represents the College on the ad hoc workgroup. This ad hoc panel met in October and coding for CTC was supposed to proceed through this panel that included representatives of all the affected GI societies and the ACR as well as observers from CMS. Both the ASGE and ACG have opted to work through the workgroup. Currently, the co-chairs of the ad hoc panel are reviewing these applications and determining next steps. Any coding applications approved by the panel at its next meeting in February would not take effect until 2009.

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International Perspective

continued from page 5

alcoholic cirrhosis, genetic hemochromatosis, primary biliary cirrhosis, and possibly alpha-1-antitrypsin deficiency, non-alcoholic steatohepatitis, and autoimmune hepatitis). Since the majority of patients at risk for HCC live in developing countries where economic constraints limit the development of surveillance programs, major efforts are needed to identify and implement cost-effective surveillance methods.

In summary, the inaugural international symposium highlighted that not only is cancer of the digestive system a worldwide problem but also that the frequency of various GI cancers differs worldwide. Although colorectal cancer is the top GI malignancy in the United States, it only ranks third worldwide in mortality after stomach and liver cancer. When caring for patients from other countries, it is important to remember that the colon may not be the only GI organ that needs to be screened.
Indication

XIFAXAN (rifaximin) Tablets are indicated for the treatment of patients (≥12 years of age) with travelers’ diarrhea caused by noninvasive strains of Escherichia coli. XIFAXAN should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than Escherichia coli.

Safety Considerations

XIFAXAN should be discontinued if diarrhea symptoms get worse or persist more than 24-48 hours, and alternative antibiotic therapy should be considered.

In clinical trials, XIFAXAN was generally well tolerated. The most common side effects (vs placebo) were flatulence 11.3% (vs 19.7%), headache 9.7% (vs 9.2%), abdominal pain 7.2% (vs 10.1%), and rectal tenesmus 7.2% (vs 8.8%).

Licensed by Alfa Wassermann S.p.A. Please see accompanying brief summary of Prescribing Information.

The Point Of A Nonsystemic Antibiotic

Works In The Gut. And Only In The Gut.
Indication

XIFAXAN (rifaximin) Tablets are indicated for the treatment of patients (≥12 years of age) with travelers’ diarrhea caused by noninvasive strains of *Escherichia coli*. XIFAXAN should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*.

Safety Considerations

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Licensed by Alfa Wassermann S.p.A.

Please see accompanying brief summary of Prescribing Information.
The effectiveness of XIFAXAN tablets was not effective in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than Escherichia coli.

**CONTRAINDICATIONS**

XIFAXAN Tablets are contraindicated in patients with a hypersensitivity to rifaximin, any of the rifamycin antimicrobial agents, or any of the components in XIFAXAN Tablets.

**WARNINGS**

XIFAXAN Tablets were not found to be effective in patients with diarrhea complicated by fever and/or blood in the stool or diarrhea due to pathogens other than Escherichia coli. XIFAXAN Tablets are not effective in cases of travelers’ diarrhea due to Campylobacter jejuni. The effectiveness of XIFAXAN Tablets in travelers’ diarrhea caused by Shigella spp. and Salmonella spp. has not been proven. XIFAXAN Tablets should not be used in patients with Campylobacter jejuni, Shigella spp., or Salmonella spp. may be suspected as causative pathogens. XIFAXAN Tablets should be discontinued if diarrhea symptoms get worse or persist more than 24-48 hours, and alternative antibiotic therapy should be considered. Pseudomembranous colitis has been reported with nearly all antibacterial agents 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 the 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 drug discontinuation 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.

**PRECAUTIONS**

**General**

The use of antibiotics may promote the overgrowth of nonresistant organisms. Should superinfection occur during therapy, appropriate measures should be taken.

**Information for Patients**

Patients should be advised that XIFAXAN Tablets may be taken with or without food. Patients should be advised that XIFAXAN Tablets should be discontinued if diarrhea persists with or without food. Patients should be advised that XIFAXAN Tablets are not effective in cases of travelers’ diarrhea due to pathogens other than

**Drug-Drug Interactions**

Although in vivo studies demonstrated the potential of rifaximin to interact with cytochrome P450 3A4 (CYP3A4), a clinical drug-drug interaction study showed no effect of rifaximin on the preexisting metabolism of an oral contraceptive containing ethinyl estradiol and norgestimate. Therefore, clinical interactions with drugs metabolized by human cytochrome P450 isoenzymes are not expected.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies were not conducted. Rifaximin was not genotoxic in the bacterial reverse mutation assay, chromosomal aberration assay, rat bone marrow micronucleus assay, and the CHO/HGPRT mutation assay. There was no effect on fertility in male or female rats following the administration of rifaximin at doses up to 300 mg/kg (approximately 5 times the clinical dose, adjusted for body surface area).

**Pregnancy—Teratogenic Effects ( Pregnancy Category C)**

**Pregnancy**

Pregnancy category C. Rifaximin was teratogenic in rats at doses of 150 to 300 mg/kg (approximately 2.5 to 5 times the clinical dose, adjusted for body surface area) and in rabbits at doses of 62.5 to 1000 mg/kg (approximately 2 to 33 times the clinical dose, adjusted for body surface area). These effects include cleft palate, agnathia, jaw shortening, hemorrhage, eye partially open, small eyes, brachymysophy, incomplete ossification, and increased thoracolumbar vertebrae. There are no adequate and well-controlled studies in pregnant women. XIFAXAN Tablets should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus.

**Use during lactation**

It is not known whether rifaximin is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for adverse reactions in nursing infants from XIFAXAN Tablets, 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**

Tablets in pediatric patients less than 12 years of age have not been established.

**Geriatric Use**

Clinical studies of XIFAXAN Tablets did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently than younger subjects.

**ADVERSE REACTIONS**

**The safety of XIFAXAN Tablets 200 mg taken three times a day (TID) was evaluated in 202 patients in two placebo-controlled clinical trials with 95% of patients receiving at least three days of treatment with XIFAXAN Tablets. All adverse events for XIFAXAN Tablets 200 mg TID that occurred at a frequency ≥2% in the two placebo-controlled trials combined are provided in Table 1.** (These include adverse events that may be attributable to the underlying disease.)

<table>
<thead>
<tr>
<th>MedDRA Preferred Term</th>
<th>Number (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fautulence</td>
<td>36 (11.3%)</td>
</tr>
<tr>
<td>Headache</td>
<td>31 (9.7%)</td>
</tr>
<tr>
<td>Abdominal Pain NOS</td>
<td>23 (7.2%)</td>
</tr>
<tr>
<td>Rectal Tenesmus</td>
<td>23 (7.2%)</td>
</tr>
<tr>
<td>Diarrhea Urgency</td>
<td>19 (5.9%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>17 (5.3%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>12 (3.8%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>10 (3.1%)</td>
</tr>
<tr>
<td>Vomiting NOS</td>
<td>7 (2.2%)</td>
</tr>
</tbody>
</table>

The following adverse events, presented by body system, have also been reported in >2% of patients taking XIFAXAN Tablets in the two placebo-controlled clinical trials where the 200 mg taken three times a day dose was used. The following includes adverse events regardless of causal relationship to drug exposure.

**Infections and Infestations:** dysentery NOS, respiratory tract infections NOS, upper respiratory tract infection NOS, skin and subcutaneous tissue infections NOS, rhinosinusitis NOS, respiratory tract infections NOS, urinary tract infections NOS

**Investigations:** aspartate aminotransferase increased, blood in stool, blood in urine, weight decreased

**Musculoskeletal and Motor Disorders:** anorexia, dehiscence Musculoskeletal, Connective Tissue, and Bone Disorders: arthralgia, muscle spasms, myalgia, neck pain

**Psychiatric Disorders:** abnormal dreams, dizziness, migraine NOS, syncope, loss of taste

**Respiratory, Thoracic, and Mediastinal Disorders:** dyspnea NOS, nasal passage irritation, nasopharyngitis, pharyngitis, pharyngolaryngeal pain, rhinitis NOS, minor coughing

**Skin and Subcutaneous Tissue Disorders:** clamminess, rash NOS, swelling increased

**Vascular Disorders:** hot flashes NOS

**Postmarketing Experience**

The following events: hypersensitivity reactions, including exfoliative dermatitis, rash, angioneurotic edema (swelling of face and tongue and difficulty swallowing), urticaria, flushing, and pruritus, have been identified during postapproval use of XIFAXAN Tablets. These events occurred as early as within 15 minutes of drug administration.

**OVERDOSAGE**

No specific information is available on the treatment of overdosage with XIFAXAN Tablets. In clinical studies at doses higher than the recommended dose (400 mg/day), adverse events were similar to the recommended dose (200 mg taken three times a day) and placebo. In the case of overdose, discontinue XIFAXAN Tablets, treat symptomatically, and institute supportive measures as required.

**Rx Only**

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January 2007

**REFERENCES**


ACG Publishes Policy Statement on Pay-for-Performance

Faced with skyrocketing health care costs and varying perceptions of “quality,” employers, health care plans, and consumers are demanding more value for their health care dollar. To counteract these spiraling expenditures with the intent to ensure better “quality,” P4P programs have been developed.

Led by ACG Past President David A. Johnson, MD, FACP, and the Quality Measures Task Force of the American College of Gastroenterology, an ACG policy statement, “Pay for Performance: ACG Guide for Physicians,” was developed to inform members of the College as to the recommended approach to the development and critical analysis of these measures. The policy statement objectives are two-fold:

1. To offer guidance to the “stakeholder” community as to the ACG leadership’s rationale and evaluation process of these proposed health care policy decisions, and
2. To provide to those parties involved in the development of P4P programs for gastroenterology, a template outline of key areas and principles that the ACG endorses as important parameters to define an appropriate process for a valid P4P program.

Some key principles the ACG endorses are that the measures be evidence-based, the measures should focus on outcomes rather than processes whenever possible, the measures should be relevant and reflect areas defined as “appropriate need for improvement,” and the measures should allow for risk adjustment and stratification bias. These are just a few of the 16 principles discussed in the article, “Pay for Performance: ACG Guide for Physicians” that you can find in the October issue of The American Journal of Gastroenterology.

Best Practices 2008

continued from page 1

Sedation.” The official course starts off at noon with Session I: Esophagus, Stomach and Duodenum, followed by Session II: Colon Cancer. After a break when you can meet and greet with exhibitors, the afternoon breakout sessions give you the opportunity to attend any two of the following sessions: Managing the GI Patient During Pregnancy, Maximizing Your Bottom Line with Ancillary Services (NPs, PAs, Infusion, ASCs, Pathology), Challenging Liver Cases in Viral Hepatitis, Approach to the Patient with Refractory Functional Disorders, Avoiding Malpractice: Risk Management in GI Practice, and Imaging in Endoscopy: NBI, Chromo and Confocal—When Are These Modalities Really Useful? The Friday program wraps up with a welcome reception.

On Saturday, Session III: Liver starts the program, followed by Session IV: Pancreas—Endoscopic Evaluation and Treatment. Following a mid-morning break, Session V will discuss Functional Gastrointestinal Disorders. Included with registration is a Saturday lunch breakout session. Attendees can choose from six options: Practice Management—Quality Measures, Benchmarking, P4P; Challenging Liver Cases in Non Viral Hepatitis; Electronic Medical Records; Complementary/Alternative Rx in Gastroenterology; Atypical Manifestations of GERD; and the Complicated IBD Patient—What Do I Do?

A keynote presentation after lunch features Scott Tenner, MD, MPH, FACP, discussing national affairs issues, their impact on you, your practice and your patients. Session VI: IBD, follows the National Affairs Keynote Session. Following a break in the program, we will repeat the sessions offered during lunch so you can attend a different presentation of interest.

On Sunday, the program wraps up mid-morning with Session VII: Therapeutic and Diagnostic Endoscopy. Use the afternoon to travel home or spend the day enjoying the beautiful resort location.


The Hyatt Grand Champions Resort & Spa, located in Indian Wells, California, is situated on a 35-acre desert oasis where you can enjoy world-class golf, tennis, swimming and more. Just minutes from Indian Wells is Palm Springs, long favored by Hollywood moguls as a recreational escape from the hustle and bustle of Los Angeles. Moderate winter weather and a beautiful setting against the backdrop of the majestic San Jacinto Mountains keeps the discriminating traveler returning to Palm Springs.

Read more about ACG’s P4P measures in the October issue of The American Journal of Gastroenterology.
ACG Never Stops Lobbying to Improve the Current Healthcare Atmosphere for GI Physicians and Patients

You want to provide the highest quality care for your patients, but the current reimbursement landscape makes it challenging. It seems that each day only brings new hurdles—insurer site-of-service policies, increasing pay-for-performance schemes, slashed Medicare rates for your services and for ASCs, etc., etc. You take care of your patients, but who takes care of you?

We do! The College is focused on the current and emerging reimbursement and policy needs of the practicing gastroenterologist, whether you have a private practice or work in an academic setting or both. Our public sector advocacy may get the most publicity and often requires your grassroots support, but we are in regular contact with private payers as well on a host of policy issues—from site-of-service payment differential schemes, to restrictive formularies to tech assessments. To see some of these communications, including, in some instances, the payers’ responses, go to http://www.acg-gi.org/members/nationalaffairs.asp#ppa.

By necessity, however, much of our attention is focused on government payers, particularly Medicare. It is no accident that it is called the 800-pound gorilla, and many of its policies are adopted by private payers. For example, private payers didn’t begin to implement site-of-service policies until Medicare did so. Many also use Medicare RVUs in setting their own payment schedules.

Getting Medicare to work better for beneficiaries and providers can be a Herculean task. First, the program essentially has a 535-member Board of Directors (the members of the House and Senate). Second, it serves a growing population of beneficiaries at a time when healthcare expenses continue to soar, the number of workers available to support the program is declining, and “budget neutrality” is the name of the game in Washington.

Congressional Environment

It is in this environment that Congress is working to enact a Medicare package in the aftermath of the months’ long attempt to reauthorize and expand the State Children’s Health Insurance Program. The President’s veto of the SCHIP package exacerbated partisan tensions and is a preview of the larger philosophical battles over healthcare that will play a significant role as we head into the 2008 elections.

Despite these machinations, no member of Congress wants to go home and tell the physicians in his or her community that he or she was unable to prevent a 10.1% Medicare pay cut in 2008. The need for an SGR fix created a mandate for a Medicare bill. At the time of this writing, a two-year physician fix is under development by the Senate Finance Committee. However, the cost of the fix (approximately $20 billion) and controversy over the necessary offsets may reduce the proposed fix to a one-year freeze. ACG has been working for months to get two key items added to this package: the “Colon Cancer Screen for Life Act” (H.R. 1926/S. 1164) and a GI-specific ASC fix. We also have worked with key policymakers and others in organized medicine to get the longest and biggest possible SGR fix enacted into law.

The Colon Cancer Screen for Life Act (SFLA) would: increase reimbursement for physicians performing colonoscopy in a facility by 30%, and by 10% in an office setting; cover the pre-operative visit for a Medicare screening colonoscopy and clarify the deductible waiver for colorectal cancer screening so that the deductible is waived regardless of the results of the screening. Co-sponsorship of the legislation stands at 75 in the House and 15 in the Senate as of this writing. Additionally, a few key champions have written Senator Baucus urging the bill’s inclusion in any Medicare package, and other Senators including Senators Ben Nelson (D-NE) and Joe Lieberman (I-CT) have put the issue on their Medicare priority lists submitted to the Finance Committee Chair. The challenging part of the legislation will be finding the necessary budgetary offsets, particularly in an environment where some policymakers may believe that a general physician fix “takes care” of everyone, but an SGR fix in the absence of action on the SFLA will ignore the fact that since the enactment of the screening benefit a decade ago, gastroenterologists have suffered a nearly 40% decrease in reimbursement for colonoscopy performed in a facility setting.

We also continue to work on enactment of a GI-specific fix to CMS’s ill-conceived final ASC rule. For simplicity sake, CMS came up with a one-size fits all rule that ignores (a) GI’s unique cost structure; and (b) the fact that reducing GI payments over four years to a level approximately 20% below costs will force procedures back into the hospital setting (a phenomenon known as reverse migration) where they cost taxpayers and beneficiaries (in the form of higher co-payments) more. “The Ambulatory Surgical Center Medicare Payment Modernization Act” was introduced months ago in the House by Representatives Kendrick Meek (D-FL) and Wally Herger (R-CA) and in the Senate, more recently by U.S. Senator Mike Crapo (R-ID). The bill would require that the payment be at least 75% of the hospital outpatient amount. While this legislation is intriguing and 75% is certainly better than the 65% specified in the final regulation, the bill would require significant offsets and is thus faces an extremely difficult road.

ACG has focused on getting a budget-neutral, GI specific fix passed that would require CMS to account for this reverse migration. CMS could pay GI more than 75% of the hospital outpatient department amount if it defined budget neutrality across all outpatient services rather than just the smaller ASC pot. In late October, we will continue to lobby for a GI-specific fix.
for example, under the leadership of ACG Montana Governor Brian Landsverk, MD, FACG, ACG held a conference call for our Montana members with one of the chief health policy advisors to Senate Finance Committee Chairman Max Baucus (D-MT) to emphasize the local impact of CMS’s proposed ASC fix. As chairman of the Senate Finance Committee, Baucus is arguably one of the—if not the most—important voices on health policy in Washington.

Coding and CT Colonography

Our concern over economic issues affecting the profession doesn’t end with legislation. The availability of a Level 1 CPT code reduces the barriers to new technology access and reimbursement, and therefore ACG has long had a seat at the CPT Advisory Committee. Currently, R. Bruce Cameron, MD, FACC, represents the ACG on this important panel which provides coding advice to the AMA CPT Editorial Panel. In October, Dr. Cameron participated in a preliminary meeting on the status of CT Colonography, as the American College of Radiology (ACR), along with the AGA, has once again pushed for a Level 1 code. At the time of this informal advisory meeting, no ACRIN data had yet been accepted for publication in a peer-reviewed journal; such publication is a requirement of the CPT process. ACG is working to understand the data and to urge that there be separate code applications for diagnostic and screening colonography if, as expected, the new evidence warrants any new code. Coding for CT Colonography will be a very hot issue in the months ahead so stay tuned. See the full article on CT Colonography on page 3.

Also on the CT Colonography front, on September 27, the College sent a letter to a Washington State tech assessment panel examining the technology. The letter noted that CT colonography does not yet meet several common tech assessment criteria. The HTA is a program created by state legislation in 2006. This program determines if health services used by state government are safe and effective. The focus of the program is to rely on scientific, or evidence-based, information about safety, effectiveness and cost to inform decisions and improve quality. An independent clinical committee will make coverage and reimbursement decisions about selected health technologies (medical equipment, devices, and diagnostic tests) based on an evidence report. These decisions apply to agencies that purchase healthcare for the State: state employee and retiree benefits, injured workers compensation, and low income residents. Technology assessments in one state or by a well-known insurer can often influence the decisions of other assessors. The assessment body will use the initial round of comments to develop more detailed questions to which ACG plans to respond.

Carrier Advisory Committee

On November 10, the National Gastroenterology Carrier Advisory Committee (GICAC) met in Washington, DC. This meeting, co-chaired by Michael Safdii, MD, FACC, Douglas Wolf, MD, FACC, and Michael Weinstein, MD, serves as the annual conference for the GI representatives to each of these carrier advisory committees (CACs) and is sponsored jointly by the three GI societies, ACG, AGA and ASGE. The ACG was well represented and the meeting agenda was loaded with key information including presentations on the current Medicare contracting reform process from the perspectives of both CMS and a former carrier medical director; an update from CMS on the Physician Quality Reporting Initiative (PQRI), and updates of CPT from ACG Governor and CPT Advisor R. Bruce Cameron, MD, FACC, and Relative-value Update Committee (RUC) from ACG member Maurits Wiersema, MD, FACC. A review of the legislative outlook for GI was also given and it included a presentation by the ACG’s Vice President of Public Policy, Julie Cantor-Weinberg.

Colorectal Screening Coverage

In addition to reimbursement issues, we know that you care about ensuring that patients are screened for colorectal cancer, but that sometimes restrictive insurance coverage policies impede patient access to screening. Recent data from the American Cancer Society and the Centers for Disease Control show that from 2002-2004, colorectal cancer incidence rates decreased by more than 2.0% per year for men and women, a decrease they attributed to be likely due to prevention through the removal of precancerous polyps. Nonetheless, only about half of American adults over 50 have been screened for colorectal cancer, far less than the percentage of women screened for cervical and breast cancer. Currently, 22 states and the District of Columbia require colorectal screening coverage by insurers operating in their states. An additional three states require colorectal screening coverage to be offered to consumers. Screening rates are significantly higher in the states that have passed coverage laws. By 2004, screening rates in states that passed colorectal cancer screening coverage laws had risen 40% faster than other states. ACG Governors are working actively in many of the states without mandates to get such mandates passed. Just this month ACG submitted comments in favor of a Pennsylvania Senate bill mandating coverage of colorectal screening.

Complementing this state-by-state approach is new legislation that would mandate coverage at the federal level. On September 25, on behalf of the College, ACG Oklahoma Governor Ralph Guild, MD, FACC, spoke at a Capitol Hill press conference in support of H.R. 3060, “The Colorectal Cancer Screening and Detection Coverage Act of 2007,” introduced by Rep. Dan Boren (D-OK, 2) who lost his mother to colon cancer. The legislation would require insurance companies to provide coverage for colorectal screening. Importantly, in defining what constitutes screening, the Boren bill references the guidelines of both the American Cancer Society and the College. 

Only about half of American adults over 50 have been screened for colorectal cancer, far less than the percentage of women screened for cervical and breast cancer.
Come for the education. Stay for the relaxation.

Keep pace with the latest GI clinical information and enjoy some R&R, by attending Best Practices 2008, an ACG/ASGE joint education program.

- Nationally recognized experts
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- Championship golf courses
- Luxurious award-winning spa
- Supervised children's programs
- Located just 15 miles from Palm Springs

Visit www.acg.gi.org for more information.
The following is a brief summary only; see full prescribing information for complete product information.

1 INDICATIONS AND USAGE

COLAZAL is indicated for the treatment of mildly to moderately active ulcerative colitis in patients 5 years of age and older. Safety and effectiveness of COLAZAL beyond 8 weeks in children (ages 5-17 years) and 12 weeks in adults have not been established.

4 CONTRAINDICATIONS

Patients with hypersensitivity to salicylates or to any of the components of COLAZAL capsules or balsalazide disodium. Hypersensitivity reactions may include, but are not limited to the following: anaphylaxis, bronchospasm, and skin reaction.

5 WARNINGS AND PRECAUTIONS

5.1 Exacerbations of Ulcerative Colitis

In the adult clinical trials, 3 out of 259 patients reported exacerbation of the symptoms of ulcerative colitis. In the pediatric clinical trials, 4 out of 68 patients reported exacerbation of the symptoms of ulcerative colitis. Observe patients closely for worsening of these symptoms while on treatment.

5.2 Pyloic Stenosis

Patients with pyloic stenosis may have prolonged gastric retention of COLAZAL capsules.

5.3 Renal

Renal toxicity has been observed in animals and patients given other mesalamine products. Therefore, caution should be exercised when administering COLAZAL to patients with known renal dysfunction or a history of renal disease.

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.

Adult Ulcerative Colitis

During clinical development, 259 adult patients with active ulcerative colitis were exposed to 6.75 g/day COLAZAL in 4 controlled trials. In the 4 controlled trials, patients receiving a COLAZAL dose of 6.75 g/day most frequently reported the following adverse reactions: headache (8%), abdominal pain (6%), diarrhea (5%), nausea (5%), vomiting (4%), respiratory infection (4%), and arthralgia (4%). Withdrawal from therapy due to adverse reactions was comparable among patients on COLAZAL and placebo.

Adverse reactions reported by 1% or more of patients who participated in the four controlled Phase 3 trials are presented in Table 1. The number of placebo patients (35), however, is too small for valid comparisons. Some adverse reactions, such as abdominal pain, fatigue, and nausea were reported more frequently in women than in men. Abdominal pain, rectal bleeding, and anemia can be part of the clinical presentation of ulcerative colitis.

Table 1: Adverse Events Occurring in ≥1% of Adult COLAZAL Patients in Controlled Trials

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>COLAZAL 6.75 g/day [N=259]</th>
<th>Placebo [N=35]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>18 (6%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14 (5%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>9 (4%)</td>
<td>0%</td>
</tr>
<tr>
<td>Nephritis</td>
<td>6 (2%)</td>
<td>0%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>0 (0%)</td>
<td>0%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0 (0%)</td>
<td>0%</td>
</tr>
<tr>
<td>Flatulence</td>
<td>5 (2%)</td>
<td>0%</td>
</tr>
<tr>
<td>Fever</td>
<td>5 (2%)</td>
<td>0%</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>5 (2%)</td>
<td>0%</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>4 (2%)</td>
<td>0%</td>
</tr>
<tr>
<td>Coughing</td>
<td>4 (2%)</td>
<td>0%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>4 (2%)</td>
<td>0%</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>3 (1%)</td>
<td>0%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3 (1%)</td>
<td>0%</td>
</tr>
<tr>
<td>Flu-like disorder</td>
<td>3 (1%)</td>
<td>0%</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>3 (1%)</td>
<td>0%</td>
</tr>
<tr>
<td>Cramps</td>
<td>3 (1%)</td>
<td>0%</td>
</tr>
<tr>
<td>Constipation</td>
<td>3 (1%)</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Adverse events occurring in at least 1% of COLAZAL patients who were less frequent than placebo for the same event were not included in the table.

Pediatric Ulcerative Colitis

In a clinical trial in 68 pediatric patients aged 5 to 17 years with mildly to moderately active ulcerative colitis who received 6.75 g/day or 2.25 g/day of COLAZAL for 8 weeks, the most frequently reported adverse reactions were headache (15%), abdominal pain upper (13%), abdominal pain (12%), vomiting (10%), diarrhea (9%), colitis ulcerative (8%), nasopharyngitis (6%), and pyrexia (6%). [see Table 2]

Table 2: Treatment-Emergent Adverse Events Reported by ≥3% of Patients in Either Treatment Group in a Controlled Study

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>COLAZAL 6.75 g/day [N=33]</th>
<th>COLAZAL 2.25 g/day [N=35]</th>
<th>Total [N=68]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>5 (15%)</td>
<td>5 (14%)</td>
<td>10 (15%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>3 (9%)</td>
<td>6 (17%)</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4 (12%)</td>
<td>4 (11%)</td>
<td>8 (12%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (3%)</td>
<td>6 (17%)</td>
<td>7 (10%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (6%)</td>
<td>4 (11%)</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>Colitis ulcerative</td>
<td>2 (6%)</td>
<td>2 (6%)</td>
<td>4 (6%)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>3 (9%)</td>
<td>1 (3%)</td>
<td>4 (6%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0 (0%)</td>
<td>4 (11%)</td>
<td>4 (6%)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>0 (0%)</td>
<td>3 (9%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>0 (0%)</td>
<td>3 (9%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Influenza</td>
<td>1 (3%)</td>
<td>2 (6%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2 (6%)</td>
<td>1 (3%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>0 (0%)</td>
<td>2 (6%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Cough</td>
<td>0 (0%)</td>
<td>2 (6%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>2 (6%)</td>
<td>0 (0%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Diarrheomelia</td>
<td>2 (6%)</td>
<td>0 (0%)</td>
<td>2 (3%)</td>
</tr>
</tbody>
</table>

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-marketing use in clinical practice of the drug or similar drugs containing mesalamine. Because these reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These adverse reactions have been chosen for inclusion due to the combination of seriousness, frequency of reporting, or potential causal connection to mesalamine.

Hepatic:

Postmarketing adverse reactions of hepatotoxicity have been reported, including elevated liver function tests (SGOT/AST, SGPT/ALT, GGT, LDH, alkaline phosphatase, bilirubin), jaundice, cholestatic jaundice, cirrhosis, hepatocellular damage including liver necrosis and liver failure. Some of these cases were fatal; however, no fatalities associated with these events were reported in COLAZAL clinical trials. One case of Kawasaki-like syndrome which included hepatic function changes was also reported; however, this adverse reaction was not reported in COLAZAL clinical trials.

Several cases of aplasia in patients taking COLAZAL have been reported.

7 DRUG INTERACTIONS

No drug interaction studies have been conducted for COLAZAL.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B. Reproduction studies were performed in rats and rabbits at doses up to 2 g/kg/day, and 4.7 times the recommended human dose based on body surface area for the rat and rabbit, respectively, and revealed no evidence of impaired fertility or harm to the fetus due to balsalazide disodium. There are, however, no adequate and 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.

8.3 Nursing Mothers

It is not known whether balsalazide disodium is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when COLAZAL is administered to a nursing woman.

8.4 Pediatric Use

A clinical trial of 68 patients ages 5-17 years has been conducted comparing two doses of COLAZAL (6.75 g/day and 2.25 g/day), [see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14)]. Based on the limited data available, dosing can be initiated at either 6.75 or 2.25 g/day.

Safety and efficacy of COLAZAL in pediatric patients below the age of 5 years have not been established.

10 OVERDOSAGE

No case of overdose has occurred with COLAZAL. A 3-year-old boy is reported to have ingested 2 g of another mesalamine product. He was treated with ipecac and activated charcoal with no adverse reactions.

If an overdose occurs with COLAZAL, treatment should be supportive, with particular attention to correction of electrolyte abnormalities.

One patient who received COLAZAL 6.75 g/day and 3 patients who received COLAZAL 2.25 g/day discontinued treatment because of adverse reactions. In addition, 2 patients in each group discontinued the study because of a lack of efficacy.

Adverse reactions reported by 3% or more of pediatric patients within either treatment group in the Phase 3 trial are presented in Table 2.

9.3 Laboratory Tests

No drug interaction studies have been conducted for COLAZAL.
SAFETY CONSIDERATIONS
COLAZAL does not relieve symptoms in all patients; your patients’ results may vary. COLAZAL was well tolerated in clinical studies. In 4 well-controlled adult clinical trials, patients most frequently reported the following events: headache (8%), abdominal pain (6%), diarrhea (6%), nausea (5%), vomiting (4%), respiratory infection (4%), and arthralgia (4%). Withdrawal from therapy due to adverse events was comparable to placebo. In the pediatric trial, patients most frequently reported the following adverse events: headache (15%), abdominal pain upper (13%), abdominal pain (12%), vomiting (10%), diarrhea (9%), colitis ulcerative (6%), nasopharyngitis (6%), and pyrexia (6%). COLAZAL is contraindicated in patients with a hypersensitivity to salicylates or to any of the components of COLAZAL capsules or balsalazide metabolites. The safety and effectiveness of COLAZAL beyond 8 weeks in children (ages 5-17 years) and beyond 12 weeks in adults have not been established.