How to avoid Kidney Stones when the weather turns hot

Intestinal Gas: Understanding is the first step to coping

Testosterone Replacement Therapy: Who can benefit?

PremierHealth

The experience you need... the compassion you deserve

SUMMER 2012

Now, we've got Newburgh covered

The magazine of PREMIER *medical group of the Hudson Valley*

LEADING THE WAY TO A HEALTHY HUDSON VALLEY

Premier Medical Group

Premier has Newburgh covered: Photographed down at the waterfront are the newest members of Premier's Urology Division, Dr. Paul Pomerantz *(left)* and Dr. Conrado N. Tojino, Jr. *(center)* with Dr. Arif M. Muslim of Premier's Gastroenterology Division offices in nearby New Windsor.

Premier's goal of being there, where the patients of the Hudson Valley need us, has taken another big step forward as our Urology Division expands. Now we cover the region from Newburgh to Kingston and from Fishkill to Rhinebeck. Meet the newest members of the Premier physician team on page 6.

It's not the average group practice that runs a heavy roster of clinical trials, has members who frequently present papers at national meetings of their professional organizations, or contribute to the major texts in their field. Well, Premier has never claimed to be "average." Skim our recent publications and presentations *(page 3)*, meet Premier's new manager of clinical trials and find out about some of the medical investigation underway right here in your neighborhood *(page 8)*.

Over the last 20 years, the number of people developing kidney stones has steadily climbed. It was once thought of as a "man's disease," but now women appear to be catching up. Find out what you can do to lower your risk of stone disease *(see page 13)*.

More than 300 folks turned out for the Premier Cares Foundation "Challenge Your Colon Chili Festival" last spring. Turn to page 10 for a taste of the festivities and the Foundation's message.

Premier Medical Group's multiple offices reduce the travel time needed to get the specialty care you deserve.

Urologists

With offices in Poughkeepsie, Kingston, Fishkill, Newburgh and Rhinebeck
MAIN PHONE: 845-437-5000

Mark R. Libin, MD
Daniel Katz, MD
Evan R. Goldfischer, MD, MBA, FACS
Michael Solliday, MD
Jason Krumholtz, MD
Scott Kahn, MD, FACS
Naeem Rahman, MD
Paul K. Pietrow, MD, FACS
Michael Young, MD, FACS
Walter Parker, MD
Paul Pomerantz, MD, FACS
Conrado N. Tojino, Jr., DO, FACOS

Allied Professional
Kevin Torrens, RPA-C
Frances Traver, ANP-C
Marylu Williams, FNP

Gastroenterologists

With offices in...
Poughkeepsie: 845-471-9410
New Windsor: 845-562-0740
Fishkill: 845-897-9797
Kingston: 845-471-9410

Sunil K. Khurana, MD, FACG
Peter M. Varunok, MD, FACG
Salvatore M. Buffa, MD
Robert S. Dean, MD
Khurram I. Ashraf, DO
Arif M. Muslim, MD
Sven Hida, MD
Farshad Elmi, MD

Allied Professional
Kimberly Nieves, NP
Thanh-Ho Nguyen, PA

PREMIER *medical group*

PremierHealth is published for Premier Medical Group of the Hudson Valley by Martinelli Slocum Publishing Inc.

Premier Medical Group Editor: Sinikka Sherwood [ssherwood@premiermedicalhv.com]
Creative Director: Alex Silberman • Publisher: Thomas Martinelli

The physicians of Premier Medical Group are affiliated with:
Northern Dutchess Hospital
St. Francis Hospital
St. Luke's Cornwall Hospital
Vassar Brothers Medical Center

[premier publications and presentations]

Presentation: Podium presentation at 2012 American Urological Association Annual Meeting
Title: "Efficacy and Safety of Oxybutynin Topical Gel (84 mg or 56 mg/day) in Patients With Urgency and/or Mixed Urinary Incontinence: Results of a Randomized, Double-Blind Placebo-Controlled Study"

Dr. Evan R. Goldfischer, principal investigator for Premier's Urology Division clinical trials, addressed the AUA regarding studies of a new therapy for patients with overactive bladder. The therapy employs oxybutynin, a tried and true medication.

In this trial, a new oxybutynin gel (OTG), was assessed. Because the drug is applied topically, it avoids a first pass through the GI system. As a result, patients were spared the GI side effects oxybutynin had been known for, primarily constipation.

The study enrolled patients with symptoms of urgency and/or mixed urinary incontinence (UI). Patients applied OTG 84 mg, OTG 56 mg, or placebo gel once daily to the abdomen, inner and upper thighs, or upper arm/shoulder. Study results showed that OTG 84 mg and 56 mg treatment yielded significantly greater improvement compared with placebo in daily episodes of urinary incontinence. OTG groups also had numerically or significantly greater improvement in the secondary outcome variables of daily urinary frequency and urinary voided volume.

The participants experienced no serious treatment-related adverse effects, and GI problems were not observed. Aside from showing the efficacy of oxybutynin gel, the study suggests that patients taking other drugs with similar GI side effects may be able to avoid those through transdermal application.

Note: Dr. Goldfischer's abstract has been selected for the *2012 Best of AUA/Japan Annual Meeting* to be held in Tokyo, Japan, October 12-14, 2012. The abstract will be presented by Dr. Matsumoto to young Japanese residents as part of an overall scientific lecture on Female Urology and OAB.

Publication: Campbell-Walsh Urology
Title: Evaluation and Medical Management of Urinary Lithiasis

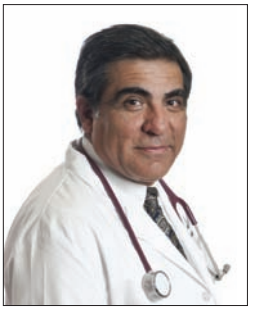
Dr. Paul K. Pietrow of Premier Medical Group's Urology Division has written the book on kidney stones. Actually, to be precise, he's written the chapter (in collaboration with Michael N. Ferrandino, MD, and Glenn M. Preminger, MD) on "Evaluation and Medical Management of Urinary Lithiasis" in the tenth edition of Campbell-Walsh Urology, internationally recognized as the preeminent textbook for the field.

Weighing in at 4320 pages (560 MB for the online edition), the book draws on the knowledge of recognized experts to cover the entire breadth and depth of the practice of urology, from anatomy through the latest diagnostic approaches and medical and surgical treatments.

"It's nice to have my work recognized," says Dr. Pietrow, "and to demonstrate that I still have my hand in academic urology." To merit his invitation to cover the subject, Dr. Pietrow regularly reviews the scientific studies and reports on trends in his area of expertise. The new edition contains updates on the dietary aspects of kidney stones and approaches to prevention.

Read Dr. Pietrow's advice on how to avoid kidney stones on page 13 of this issue of *PremierHealth* magazine.

Presentation: 2011 American College of Gastroenterology Annual Meeting
Title: Th1 & Th17/Treg-rebalancing by small molecule Natura-α shows great promises against ulcerative colitis in a randomized, double-blind, placebo-controlled Phase II clinical trial



Dr. Sunil K. Khurana, Premier's principal investigator for clinical studies relating to inflammatory bowel disease, presented the results of a 10-site study examining the results of treating patients with moderate to severe ulcerative colitis with varying doses of Natura-α.

Inflammatory bowel disease is thought to result from an aberrant intestinal immune response involving disequilibrium between regulatory T cells (Treg) and pro-inflammatory Th17 cells. Natura-α is a synthetic small molecule meant to reestablish immune system balance by increasing Treg and decreasing Th17 cells.

Results of the randomized, double-blind, placebo-controlled study suggested that Natura-α shows highly and statistically significant therapeutic effect in treating patients with moderate-to-severe ulcerative colitis. Not only did the treatment prove safe and well-tolerated by patients, there were indications, the study concluded, that it "may be equally effective in patients non-resistant/non-intolerant to as well as previously resistant/intolerant to 5-ASA, steroids, immunosuppressants or biologic therapies."

The ACG audience of physicians was excited by the possibility that targeting the Treg and Th17 cells may be an effective therapeutic strategy not only for ulcerative colitis but also for a variety of autoinflammatory/autoimmune diseases.

Publication: Patient Preference and Adherence, Nov. 2011
Title: Evaluation of pharmacokinetics, user handling, and tolerability of peginterferon alfa-2a (40 kDa) delivered via a disposable autoinjector device

Dr. Peter M. Varunok, principal investigator for Premier's GI Division clinical trials, was the lead author on this first study to examine the use of auto-injectors for patients self-administering hepatitis C drugs.

"Interferon, a current mainstay of hepatitis C medication, requires a weekly injection, and there were difficulties with that," says Dr. Varunok. "Some people have needle-phobia. There can be technical difficulties in self-adminstering the injection properly and errors occur that can affect their dosage, which in turn, can effect their response rate. For people with a prior history of drug use, the use of needles has brought up fear of relapsing."

The pre-filled autoinjector lets patients administer the medicine with the push of a button. The study found that, after a brief period of adjustment, patients were "more satisfied and confident, followed instructions better, and successfully initiated injection with the autoinjector versus the pre-filled syringe."

The paper finds: "By improving convenience and shielding the needle from view, findings from this study suggest the autoinjector may have the potential to help patients overcome injection-related problems, such as pain/discomfort, anxiety, fear of needles, fear of recidivism, and worry over incorrect injection techniques, all of which may improve patient adherence to study medication, which can subsequently increase the potential to achieve viral suppression."

Note: The pre-filled autoinjector has become the preferred medication delivery system in the hepatitis C community.

PREMIER CARES FOUNDATION

Third Annual Prostate Cancer Walk

Walkway Over the Hudson [Highland side]

Saturday, September 29, 2012

- Registration: 9–9:45am
- Walk: 10–11am
- Followed by awards ceremony and refreshments

Premier Cares Foundation is committed to assisting our fellow community members get access to free prostate cancer screenings and cancer treatment.

The Walk presents an unmatched opportunity for community leaders, businesses and individuals to provide financial support to those men and families touched by prostate cancer. It also is the only men's health fundraiser in the Hudson Valley!

Last year over 700 people participated in the Walk, raising over $100,000, and also raising awareness of the importance of dealing with prostate cancer.

The support of community leaders, businesses and organizations can help us meet our goal. There are numerous sponsorship levels available, all tax deductible, as allowed by law.

Individuals can support this important cause by signing up to participate in an exhilirating morning walk with the entire family. Enjoy the magnificient views from the Walkway Over the Hudson, soaring 212 feet above the Hudson River. There will be entertainment, refreshments, and great prizes. Funds raised will be donated to local charities for a range of prostate cancer programs.

- Registration Fee: $20 per person. Pre-registered participants are guaranteed a free T-shirt and goody bag.
- Children under 12 are free (T-shirt and goody bag not included).

To Register Online: premiercaresfoundation.ticketbud.com/prostatecancerwalk2012

For event questions: Contact Julie Goldfischer, Executive Director of Premier Cares Foundation; jgoldfischer@premiercaresfoundation.org or call 845.453.1160

For registration questions: Contact Monica Metty at mmetty@premiercaresfoundation.org or call 845.656.7325

The Pathologists are in

Having an in-house pathology lab guarantees that Premier's labwork is done promptly and efficiently—with two pathologists reviewing every "positive" specimen— so our patients won't have to endure anxious waits to learn about the next step in their treatment.

What is the major benefit of having a dedicated "in-house" pathology department? On this question, the physicians at Premier Medical Group are all agreed: **The Time Factor.**

"If I do a colonoscopy or endoscopy to remove a polyp or biopsy a lesion and I expect it might be a cancer, I can tell our lab I need the results tomorrow, not two days from now," says Dr. Sunil Khurana of the GI Division. "This is especially significant if there's a weekend approaching. Let's say you do a colonoscopy on Thursday and you take a biopsy. If it goes to an outside lab, the earliest you'll get it back is Monday or Tuesday. And that leaves the patient thinking—for five days—do I have it, do I not have it, what do I do? In the great scheme of things, perhaps four or five days doesn't really matter for the course of the cancer. But psychologically and emotionally, it matters a lot. Four days is a lot of time to spend worrying. With the fast turnaround of our pathology department, we can tell our patient something decisive on Friday morning."

The second major benefit is in the realm of quality, and this quality takes several forms. First, having two pathologists on staff means that specimens that come back positive for cancer, or anything abnormal, are double read. When a cancer-positive report comes back to a physician, we know it has been discussed and confirmed or singled out for further examination.

Our confidence in the quality of the pathology reports is enhanced by the fact that our reading pathologist has 25-years experience in reviewing gastrointestinal and genitourinary specimens. In a large hospital or a big lab, pathologists handle a wide range of specimens, including skin lesions, colon tissue, lung biopsies, etc. A big medical center may have subspecialist pathologists on staff, but in a community hospital, it's usual for the pathologist to examine everything and anything.

At Premier, concentration on GI and GU specimens allows the pathologist to acquire and refine the necessary medical knowledge and diagnostic skills needed to make the right call, over and over again.

Our close relationship with the pathology lab gives physicians the opportunity to communicate directly with the lab's tech staff. When a biopsy is sent out to a commercial lab, all you can expect is that they'll "process" it. At Premier, if something about the biopsy, or the circumstance of taking it, looks or feels "different," the physician can ask for a custom review that takes anomalies into account.

We are also able to work with our pathologist to customize testing parameters that provide information that may be more meaningful to the physician, and patient treatment, than the standard protocol.

Dr. Leon Isaac, MD, is Medical Director of Premier's Pathology Department. His attention to staffing, quality control, and strict adherence to professional and regulatory requirements has garnered him many awards. Dr. Martin Davidson is the primary reading pathologist.

Premier's well-trained technicians (below) are responsible for accessing and processing specimens and microbiology. The results, slides or machine generated reports, are then provided to the pathologists for review.

[premier is there, where you need us]

New in Newburgh

Dr. Pomerantz and Dr. Tojino continue caring for their patients in Newburgh, as members of the Urology Division of Premier Medical Group of the Hudson Valley.

"Joining forces gives us the opportunity to expand our offerings and technical expertise from Newburgh to Poughkeepsie to Fishkill to Rhinebeck to Kingston. The Premier brand and Premier quality truly covers the Hudson Valley."

By the time you read this issue of *PremierHealth* magazine, a new merger of medical practices will have extended Premier service and Premier quality in urology to the Newburgh area, where Dr. Arif Muslim has long represented Premier as a leading gastroenterologist. Mid-Hudson Urological Associates has joined forces with Premier Medical Group of the Hudson Valley to ensure, as Dr. Paul Pomerantz expresses it, that patients in the region will be able to benefit from the high-tech and institutional processes that characterize 21st century medicine at its best.

"In Mid-Hudson Urological Associates, we saw a solid practice and two talented physicians who have served the area for quite some time," says Dr. Evan Goldfischer, co-managing director of Premier. "Dr. Pomerantz has been practicing there for 30 years plus; Dr. Tojino has cared for patients in Newburgh, his hometown, for almost 15 years.

"Joining forces," says Goldfischer, "gives us the opportunity to expand our offerings and technical expertise from Newburgh to Poughkeepsie to Fishkill to Rhinebeck to Kingston. The Premier brand and premier quality truly covers the Hudson Valley."

We are very pleased about our merger with Premier Medical Group," says Dr. Paul Pomerantz, "and expect it to be a good fit. We pride ourselves on practicing good medicine and the doctors at Premier, who I've known over the years, practice a good version of urology as well.

"Premier" says Pomerantz, "brings a depth of expertise and administrative know-how that we don't have on our own. In today's health care environment, it's nearly impossible for a smaller practice to master all the technologies that come down the pike and to be able to comply 100 percent with various and sundry governmental bodies, insurance carriers, and other health care organizations that interact with us. I definitely think the introduction of Premier's high-tech and institutional processes will really enable us to practice the best of 21st century medicine. Being able to interact with physicians who are well-versed and well trained in various aspects of urology—friendly, non-competitive, and accessible— is going to be a help for everyone, patients and physicians.

"The merger," says Pomerantz, "allows us, as part of Premier, to provide urology care to a larger segment of the Hudson Valley. Frankly, there have not been enough urologists in this area. Roddy and I have basically provided the bulk of urology care here. While I think we provide a high level of quality medicine, we've been limited by the fact that there are only two of us, and there are a lot of people to take care of." The merger, according to Pomerantz, "has already helped us attract new urologists, very highly-trained individuals, to help provide care for folks on this side of the river."

Will Mid-Hudson Urology Associates' patients notice and appreciate the change? "The type of personal care we deliver is not going to change markedly," says Pomerantz. "We live in the community, we know a lot of the people in the community, and that is not going to change. Certainly, to start with, the outward appearance will be a bit different. We have a different logo and the phones are being answered differently. Our patient information will be gathered into more complete electronic medical records. Premier has a system that includes pre-visit interviews, something we haven't be able to do before, which provides a great deal of advance information that's very helpful to the doctors. Hopefully, this will permit visits to be more productive and efficient for the patient. As far as I'm concerned, this merger sounds like something that's going to work."

Premier has had an excellent reputation in the area, and they have their act together," says Dr. Conrado Tojino, "so we're excited about this merger. We're excited about being part of a team that conducts clinical research, part of a team that's been very efficient with their business practice. We're also looking forward to getting some more help in this area. Dr. Pomerantz and I have been the only two urologists in the eastern part of Orange County, where there should be five or six urologists. So we're inundated with patients."

Among the first benefits of merging with Premier is being able to recruit two fine fellowship-trained urologists, who will be starting with the group in August. "That means that patients will be able to get first-rate urology care in a more timely fashion," Tojino says. "Until now, they've sometimes had to wait three to six weeks to see us. Along with Premier's policy of providing nurses to answer patient questions on the phone, the benefits to our patients will be great."

Senior Physicians

Paul Pomerantz, MD, FACS

Conrado N. Tojino, Jr., DO, FACOS

New Members of Premier's Newburgh Team

Dr. Praneeth Vemulapalli received his MD, with research honors, from Tufts University School of Medicine in 2005. He completed a six-year urology residency at SUNY Stony Brook University Medical Center, finishing as Chief Resident of the Department of Urology.

He comes to Premier Medical Group directly from Ohio State University Medical Center, James Cancer Center, where he was awarded the prestigious Clinical Fellowship in Robotic Urologic Surgery for 2011-2012.

Dr. Vemulapalli has contributed to papers published in The Journal of Urology, and the Journal of Cellular Biochemistry. He has delivered poster presentations for the American Association for Cancer Research and the American Society for Reproductive Medicine.

Dr. Jaspreet Singh received his DO from the NY College of Osteopathic Medicine in 2003 and did his residencies in General Surgery and Urology at Albert Einstein Medical Center and Philadelphia College of Osteopathic Medicine, respectively.

He comes to Premier from a position as Assistant Professor at Thomas Jefferson University Hospital, where he has served on the faculty since 2009 and was Fellowship-trained in Urologic Oncology. He has contributed to numerous papers on the management of prostate cancer and is currently engaged in several research trials investigating approaches to metastatic prostate cancer. A frequent guest lecturer on a wide range of urologic issues, Dr. Singh has also delivered a number of podium presentations and abstracts at national AUA and other professional society meetings.

Kimberly Secord, RN, CCRC
Clinical Research Manager

"As Clinical Research Manager my workday is split between administrative and regulatory duties and patient care. I've been a nurse for 20 years and I don't ever want to stop seeing patients.

Frankly, I love the nature of this work. Research gives me the opportunity to contribute in a team setting, become involved with up-and-coming medicines and treatments and, perhaps most of all, to have new options to offer patients.

I love the extra TLC the patients get, that one-on-one interaction. If they need a half hour to sit and talk to you, they get the half hour. It's kind of why you become a nurse in the first place. You want to take care of the patient both physically and emotionally, and in this kind of job you have the chance to do that.

Clinical research is necessary for the world of medicine to continue to improve and grow.

Exploring new options that redefine the possible treatment of disease and improve quality of life is what I do as a Certified Clinical Research Coordinator. I'm gratified to know it makes a difference."

Finding a Better Way

The doctors and research staff of Premier Medical Group of the Hudson Valley continue their engagement in clinical trials in the hope of finding the newest, most effective treatments for their patients.

Between the Urology Division and the Gastroenterology Division, it's not unusual for two to three dozen clinical trials to be underway at any given time at Premier Medical Group of the Hudson Valley. More than a dozen years of first-rate, dependable trial management has earned Premier the kind of trust and reputation that draws many requests for its participation in investigatory work.

After serving as a Certified Clinical Research Coordinator and manager of the research wing of the Urology Division, Kimberly Secord, RN, CCRC, was appointed Clinical Research Manager of Premier's combined research effort. Since May 1, 2012—with the research units joined as a single team—the considerable task of orchestrating budgets, contracts and a blizzard of regulatory requirements—as well as managing adherence to the practices required to stay in compliance with GCP (Good Clinical Practice) and FDA guidelines— all fall on her shoulders.

Premier Medical Group's Research Department has participated in clinical trials leading up to the approval of drugs such as Viagra, Levitra, Cialis, Detrol LA, Vesicare, Sanctura, Gelnique, Rapaflo, Firmagon, Xgeva and Pegasys ProClick.

Some of the regulatory requirements and guidelines Secord oversees are meant to protect the scientific integrity of the clinical trials' data. Many regulations serve to safeguard the health and privacy of patient participants. Secord's 20 years as a RN has led her to firmly place the patient as a top priority.

"Our first contacts with a patient involve discussions that can lead to informed consent," says Secord. The studies are carefully explained so that the patient fully understands the potential benefits and potential risks, and is made aware that he or she is free to stop participating at any time.

"Research patients," says Secord, "get an extra bit of TLC. They have a clinical research coordinator dedicated to them, someone they can call and e-mail, and get almost instant responses from."

Recent clinical trials at Premier have touched on just about every disease state that might be treated in a urology or GI office. New pharmaceuticals, "natural" supplements, drug delivery systems, and non-drug treatments have been investigated for erectile dysfunction, interstitial cystitis/painful bladder syndrome, BPH, overactive bladder, nocturia, vaginal atrophy, female sexual dysfunction, and prostate, bladder and kidney cancer.

Frequently, there are several new drugs and drug regimens for Crohn's disease being studied at the same time, as well as treatments for irritable bowel, ulcerative colitis, hemorrhoids, constipation, and extensive investigations in hepatitis C regimens.

The Research Department has long been involved in studying the next generation of therapies for many disease processes.

The side effects of many medications constitute a significant challenge, making it difficult for some patients to complete the full course of a specific standard treatment, even eliminating some from the possibility of cure. New approaches may overcome the barriers presented by the side effects, which will allow successful treatment of more patients.

Many of the clinical trials conducted at Premier have resulted in real-life success stories. Numerous opportunities for treatment have been made available to Premier's patients, oftentimes providing benefits from medications and procedures long before they have come to market and been adopted as the new standards of care.

In many cases, participating in clinical trials has given Premier the opportunity to provide its patients with something better.

New CDC guidelines: All baby boomers should get tested for hepatitis C

Official CDC Press Release — The Centers for Disease Control and Prevention is issuing draft guidelines proposing that all U.S. baby boomers get a one-time test for the hepatitis C virus. One in 30 baby boomers – the generation born from 1945 through 1965 – has been infected with hepatitis C, and most don't know it. Hepatitis C causes serious liver diseases including liver cancer, which is the fastest-rising cause of cancer-related deaths, and the leading cause of liver transplants in the United States.

CDC believes this approach will address the largely preventable consequences of this disease, especially in light of newly available therapies that can cure up to 75 percent of infections.

"With increasingly effective treatments now available, we can prevent tens of thousands of deaths from hepatitis C," said CDC Director Thomas R. Frieden, M.D., M.P.H.

More than 2 million U.S. baby boomers are infected with hepatitis C, accounting for more than 75 percent of all American adults living with the virus. Baby boomers are five times more likely to be infected than other adults. Yet most infected baby boomers do not know they have the virus because hepatitis C can damage the liver for many years with few noticeable symptoms. More than 15,000 Americans, most of them baby boomers, die each year from hepatitis C-related illness, such as cirrhosis and liver cancer. Deaths have been increasing steadily for over a decade and are projected to grow significantly in coming years.

FAQs for Baby Boomers

- **One in 30 baby boomers has been infected with hepatitis C, and most don't know it.**
- **Newly available therapies can cure up to 75 percent of infections.**
- **More than 15,000 Americans, most of them baby boomers, die each year from hepatitis C-related illness,**
- **One-time hepatitis C testing of baby boomers could identify more than 800,000 additional people with hepatitis C, prevent the costly consequences of liver cancer and other chronic liver diseases and save more than 120,000 lives.**

"Identifying these hidden infections early will allow more baby boomers to receive care and treatment, before they develop life-threatening liver disease," said Kevin Fenton, M.D., director of CDC's National Center for HIV/AIDS, Viral Hepatitis, STD and Tuberculosis Prevention.

Current CDC guidelines call for testing only individuals with certain known risk factors for hepatitis C infection. But studies find that many baby boomers do not perceive themselves to be at risk and are not being tested.

CDC estimates one-time hepatitis C testing of baby boomers could identify more than 800,000 additional people with hepatitis C, prevent the costly consequences of liver cancer and other chronic liver diseases and save more than 120,000 lives.

FUNDS AND AWARENESS RAISED AT OUR FIRST

Challenge Your Colon Chili Festival

Over 300 people gathered at the Poughkeepsie Grand Hotel on March 25, 2012, to attend Premier Cares Foundation's first annual "Challenge Your Colon Chili Festival: Celebrating the Local Culinary Flavors of the Hudson Valley."

The Festival is slated to be a regular observance of Colon Cancer Awareness Month. By the time this first event was over, a lot of great chili and local food and beverages had been consumed, some important messages about health and community had been brought home to the Hudson Valley, and more than $36,000 had been raised to help the Foundation carry on its work.

This family friendly event was made possible by the generous contributions of local restaurants, bakeries, breweries, vintners and vendors who gave of their time and talent. Stolen Heart, the Dutchess-County-based country music band, performed while the kids enjoyed pasta tastings and a variety of crafts and activities and the adults savored tasting portions of prize chili recipes and other local delicacies.

A panel of chefs from the Culinary Institute of America served as official judges for the chili contest, while everyone got to vote to select the "people's choice." (See page 12 for results.)

"This was truly a great event, bringing even more public awareness to the importance of early screenings in the fight against colon cancer," said Dr. Sunil Khurana, Co-Chief Executive Officer of Premier Medical Group and a Premier Cares Foundation Board Member.

Proceeds of this event will benefit Premier Cares Foundation, a 501(c)3 charity whose mission is to provide support, education, awareness, and treatment for those individuals in the community lacking sufficient funds to address significant urologic and digestive diseases including prostate and colon cancers.

For more information contact Executive Director Julie Goldfischer at 845-453-1160 or jgoldfischer@premiercaresfoundation.org.

This family friendly event was made possible by the generous contributions of local restaurants, bakeries, breweries, vintners and vendors who gave of their time and talent. Thank you!

Photos by Wendy Sbrollini / KEE Photography

Dr. Salvatore M. Buffa of Premiere's GI Division with daughter Siena (left) and her friend Amy Ryan, both of whom volunteered to help out.

"I believe the community's participation in this year's Colon Cancer Awareness event, the Challenge Your Colon Chili Festival, shows that we've had some success in spreading our message. But important as our message is—that colonoscopies and early detection of colon cancer can save lives—we could always do with more awareness.

We wanted to make this a family-oriented event because keeping your family members healthy is of paramount importance and ultimately makes for a happier community. According to the people who were there, the event was extremely well-run. The vendors did a great job with the food and drink. The speakers did a great job of making people aware of the importance of screening. Even all the kids had a great time with the music and games.

Most important, of course, is that the Foundation was able to raise funds for its projects and that we were able to offer free colonoscopies to people who truly wanted them but didn't have the means to get them on their own." —Dr. Salvatore M. Buffa

SAVE THE DATE: NOVEMBER 10, 2012
The 2nd Annual Celebrity Chef Dinner

Premier Cares Foundation's second annual Celebrity Chef Dinner, entitled "Re-Elect White House Chef Walter Scheib," will be held on Saturday evening, **November 10, 2012.**

Chef Scheib returns to the Hudson Valley during election month, this time preparing a multi-course State Dinner featuring specialty cuisines he has prepared for some of the most memorable guests during his tenure at the White House, including Tony Blair, Nelson Mandela and Lady Diana Spencer.

Chef Scheib will be holding a Master Chef cooking class and a small cocktail party for top sponsors of the Premier Cares Foundation fundraiser during the weekend.

For more information contact Executive Director Julie Goldfischer at 845-453-1160 or jgoldfischer@premiercaresfoundation.org.

Bernadette Pikul was one of many Hudson Valleyites to send in an essay describing her need for a free colonoscopy. Her essay, which she's permitted us to share with readers, shows why the work of the Premier Cares Foundation is so necessary. The essay has been edited for length.

My Story

On April 1, 2012, I will be a 3-year breast cancer survivor. I was diagnosed at the age of 49 and have undergone chemotherapy, lymph node removal, lumpectomy, mastectomy, plastic surgery and radiation... Although I had always been an advocate of preventive health, before the BC diagnosis, I had not gone for my yearly mammogram and pap smear in 3 years....

A lot of the reason had to do with money since I could not afford medical treatment and paying out of pocket... At the age of 52, I know that I am due to have a colonoscopy screening, but I am again hesitant due to the financial hardship this may cause. In March 2010, while I was going through all of this [cancer treatment], my position was eliminated at a company that I worked at for over 25 years. I am now working full-time, but my salary is almost half the amount it was. Needless to say, it is becoming difficult to make ends meet. My husband works full-time, but we have 4 children under the age of 15...

"I would hate to be another statistic just because I could not afford preventive health care. Thank you for listening to my story... Thank you for offering this service and doing your part to raise awareness and save lives."

It is sad because we are middle class, hard-working people who have worked all our lives, never ask for hand-outs, do not live outside our means, but yet we are struggling financially. Having a free screening would be a very big help... I am sure there are many people out there in the same boat, given today's economy, but I would hate to be another statistic just because I could not afford preventive health care. Thank you for listening to my story... Thank you for offering this service and doing your part to raise awareness and save lives.

Bernadette Pikul

PREMIER AWARD FOR BEST CHILI

Cosimo's

Habanero Award
{1st runner-up for Best Chili}

La Puerta Azul

Jalapeno Award
[2nd runner-up for Best Chili}

Crew

PEOPLE'S CHOICE AWARD FOR BEST CHILI

Crew

Poblano Award
{People's Choice runner-up}

Bangall Whaling Company

The Real Winners:

Your friends and neighbors in the Hudson Valley who will be educated, treated, and helped through the work of the Premier Cares Foundation.

WHAT YOU NEED TO KNOW TO AVOID

Kidney Stones

The hot days of summer bring on a rise in the number of people going to their doctors or the emergency room for help with the pain of kidney stones. Staying hydrated by drinking enough water to replenish fluids lost through heat and exertion is the crucial step to staving off this common urological problem.

Paul K. Pietrow, MD, FACS

There are three things you should know about kidney stones.

1. They can be very, very painful.
2. Currently, about one in 11 Americans get kidney stones. There are 600,000 emergency room visits annually for the condition. This is nearly double the incidence of stone disease just 15 years ago, and the numbers of people affected continues to rise.
3. Most people can reduce the risk of getting a first, or even a repeat, kidney stone by following relatively simple dietary and lifestyle measures.

The what and why of kidney stones

Simply put, a kidney stone is a hardened mineral deposit that develops from crystals that have separated from the urine within the urinary tract. These crystals form due to an imbalance between fluid and certain wastes that urine is meant to dispose of. The result is a high concentration of mineral salts that do not dissolve.

Most of these tiny particles make their way out of the urinary tract unnoticed. Sometimes, however, they can settle on an inner surface and build, layer by layer, until they form stones.

Urine naturally contains chemicals that prevent or inhibit the crystals from forming. But in some people, these inhibitors do not fully function, making them genetically predisposed to forming stones.

Drinking enough water helps keep urine diluted, flushes away materials that might form stones and is the most important thing a person can do to prevent kidney stones.

Men are more likely to develop kidney stones than are women. "The ratio used to be three to one; it's just under two to one now," says Dr. Paul Pietrow, a kidney stone specialist in Premier's Urology Division. "Gender and genetics have always played a role in kidney stones. Now women are catching up… why? It's most likely related to a degradation in diet. It turns out that obesity is its own independent risk factor for stones. As more women get obese and adopt worse diets, they get to catch up to their stone-forming male counterparts."

People who have had a kidney stone—and do not work toward prevention with dietary means or medical treatment—have a 50 percent chance of a recurrent stone within ten years of the first.

The stone friendly diet

"A poor diet, in relation to kidney stones, involves several things," says Pietrow. "One of those is protein. We know that consuming high volumes of animal protein increases uric acid in the urine, which raises the risk of uric acid and calcium stones.We advise stone formers to consume no more than 6 ounces of animal protein a day.

"Salt also has a significant effect," says Pietrow. "Packaged, canned and prepared foods are all high in sodium, which drags calcium into the urine. There, it binds with oxalate, and can develop into the most common type of stone, calcium oxalate.

"You can't avoid oxalates completely," Pietrow notes, "since all fruits and vegetables have some. But you should avoid foods with a very high oxalate content, such as spinach, swiss chard, rhubarb, hot cocoa, roasted peanuts and strong tea." Consulting an oxalate chart will help you make wise food choices. And if you do consume a high-oxalate food, drinking plenty of water along with it will help flush the oxalate out.

"Drink plenty of fluids; watch out for salt; monitor the animal protein; avoid heavy oxalate loading; get calcium as dairy with your meals and increase citrate in your diet… that's the standard "You've had a stone, don't make another one" talk.

The preventive foundation for people who we know make stones is to drink plenty of fluids. Everything else gets built on top of that. Their target is to produce about 2 quarts of urine daily.

If you haven't yet been identified as a stone-former, you still need to keep yourself reasonably hydrated. Your urine shouldn't get really dark and concentrated, but it doesn't have to be crystal clear all the time either, just on the lighter side of yellow.

Citrate is a natural stone-preventer. Of the fruit juices, lemon has more citrus, ounce for ounce, than anything else. I tell people who make stones to squeeze some lemon into water and keep a pitcher of that in the fridge. Orange is good too.

For people who have had repeat bouts of stones we might do a metabolic evaluation, including blood and urine tests, to help pinpoint why they are making stones. In some cases we'll consider using medications that can change the makeup of the urine and moderate or eliminate the conditions that bring on kidney stones."

WHAT YOU NEED TO KNOW ABOUT

Testosterone Replacement Therapy

There's no need to just give in to aging: sex drive, energy levels, memory and mental acuity may all be increased for men who suffer from "low-T."

Evan R. Goldfischer, MD, FACS

Testosterone is the most important male sex hormone. Produced predominantly in the testes, it's testosterone that fires up the male characteristics that come to the fore at puberty, from a deepening voice and increased body hair to increased muscle strength and sexual drive.

Testosterone peaks in early adulthood, and the levels gradually decline with age—about 1 percent a year after age 30. Diseases (such as diabetes), accidents and certain drugs (such as anti-depressants) also lower testosterone levels. The NIH estimates that about 5 million American men have low testosterone (low-T).

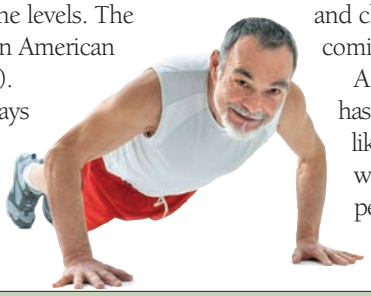
"Men with low testosterone," says Dr. Evan Goldfischer, "don't just notice a decrease in their sexual desire, they also experience a decrease in their energy levels, memory and mental acuity. A lot of men just chalk it up to aging."

But just as with aging or disease, it's not necessary to simply give in to the effects of low testosterone. Ever since the 1939 Nobel Prize in Chemistry was awarded for the synthesis of testosterone, scientists have investigated and developed testosterone replacement.

"Up to a decade or so ago," says Dr. Goldfischer, "men had to get injections every one to three 3 weeks. The deep muscle injections were painful and the body's testosterone levels had significant fluctuations, with noticeable highs and lows."

Then, testosterone gels became available, some of which Premier's research division played a part in developing. "Applying gels on a daily basis to reach more normal T-levels became appealing," says Goldfischer.

Gels are easy to apply and don't cause the fluctuation of T-levels that come with injections. The skin absorbs the testosterone quickly, stores it and releases it slowly into the blood. On the down-side, the gels can cause skin irritation, itching or blisters. More significantly, women and children must be prevented from coming into contact with the gel.



A new alternative, testosterone pellets, has been developed for men who don't like the gel or aren't able to comply with the daily application. "The pellets are implanted under the skin in our offices," says Goldfischer. "It takes about 5 minutes to do and provides sustained levels of testosterone for about four months.

"We currently have quite a few patients on testosterone replacement," Goldfischer adds. "Frankly, we're relieved when men are coming to us for drugs that are FDA approved, not the shady stuff advertised on TV or unregulated supplements from the vitamin shop."

Testosterone supplementation has definite risks and possible side effects. Premier advises patients on testosterone replacement therapy to come into the office every three or four months for blood tests and a review of prostate and liver health.

Low Testosterone?

If you're experiencing a lack of interest or desire in sexual activity, take this simple questionnaire and discuss the results with your doctor.

Answering yes to questions 1 or 7, or any 3 other questions, may signal you have low testosterone, which can be confirmed with a simple blood test.

1. Do you have a decrease in sex drive?	YES	NO
2. Do you have a lack of energy?	YES	NO
3. Do you have a decrease in strength and/or endurance?	YES	NO
4. Have you lost height?	YES	NO
5. Have you noticed a decreased "enjoyment of life"	YES	NO
6. Are you sad and/or grumpy?	YES	NO
7. Are your erections less strong?	YES	NO
8. Have you noticed a recent drop in your ability to play sports	YES	NO
9. Are you falling asleep after dinner?	YES	NO
10. Has there been a recent decline in your work performance?	YES	NO

"When a patient comes to see us about erectile dysfunction (ED), one of the first questions we ask is, 'do you experience strong sexual desire?' If the answer is yes, they do have desire but don't have satisfactory erections, the problem to deal with is most probably vascular or neuorgenic in origin.

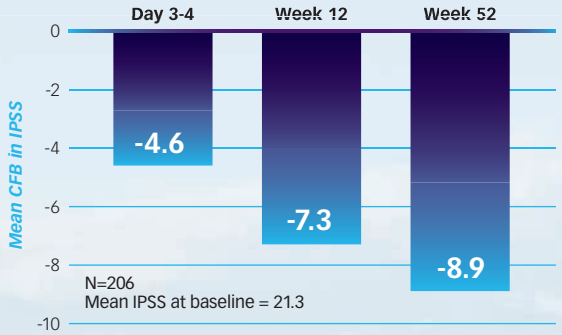
But if the patient tells us that his sex drive has declined, or that he rarely experiences sexual desire, that could be a sign of problems with his testosterone levels and, possibly, other hormones as well.

There are so many things that go into sexual functioning. The human brain, not the penis, is the most powerful sexual organ. We ask our patients about their stress factors, strains in the relationship, money worries, all of which can have an impact on sex drive. But ultimately, even if everything else is going right, if a man's brain isn't sufficiently bathed in testosterone, he won't experience satisfactory erections.

Today, testing and treatment for low testosterone are easy to do. There are several ways to accomplish testosterone replacement and bring the levels up. Each method has its pros and cons and we help our patients decide on which will suit their lifestyle best."

AVOID THE STOP AND GO OF BPH

Mean change from baseline (CFB) in IPSS* total score[1,2†]



†Data from patients who received RAPAFLO® for 12 weeks in a double-blind, placebo-controlled trial and for an additional 40 weeks in an uncontrolled, open-label extension study.

Continued BPH‡ symptom relief over 1 year†

*International Prostate Symptom Score
‡Benign prostatic hyperplasia

RAPAFLO® is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH). RAPAFLO® is not indicated for the treatment of hypertension.

Important Safety Information

RAPAFLO® is contraindicated in patients with severe renal impairment (CCr <30 mL/min), severe hepatic impairment (Child-Pugh score ≥10), and with use of strong CYP3A4 inhibitors.

Postural hypotension with or without symptoms (eg, dizziness) may develop when beginning treatment with RAPAFLO®. As with all alpha-blockers, there is a potential for syncope. Patients should be warned of the possible occurrences of such events and should avoid situations where injury could result. RAPAFLO® should be used with caution in patients with moderate renal impairment. Patients should be assessed to rule out the presence of prostate cancer prior to starting treatment with RAPAFLO®. Patients planning cataract surgery should inform their ophthalmologist that they are taking RAPAFLO®.

The most common side effects are retrograde ejaculation, dizziness, diarrhea, orthostatic hypotension, headache, nasopharyngitis, and nasal congestion.

Please see brief summary of full Prescribing Information on adjacent page.

Models are for illustrative purposes only.

www.rapaflo.com

References: 1. Marks LS, Gittelman MC, Hill LA, Volinn W, Hoel G. Silodosin in the treatment of the signs and symptoms of benign prostatic hyperplasia: a 9-month, open-label extension study. *Urology.* 2009; 74:1318-1322. **2.** Data on file, Watson Laboratories, Inc.

RAPAFLO® 8 mg (silodosin) capsules

READY. SELECT. GO.

Watson

RAPAFLO®
(silodosin) capsules

BRIEF SUMMARY

For full Prescribing Information, see package insert.

INDICATIONS AND USAGE

RAPAFLO, a selective alpha-1 adrenergic receptor antagonist, is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH). RAPAFLO is not indicated for the treatment of hypertension.

CONTRAINDICATIONS

- Severe renal impairment (CCr < 30 mL/min)
- Severe hepatic impairment (Child-Pugh score ≥ 10)
- Concomitant administration with strong Cytochrome P450 3A4 (CYP3A4) inhibitors (e.g., ketoconazole, clarithromycin, itraconazole, ritonavir) [*see Drug Interactions*]

WARNINGS AND PRECAUTIONS

Orthostatic Effects

Postural hypotension, with or without symptoms (e.g., dizziness) may develop when beginning RAPAFLO treatment. As with other alpha-blockers, there is potential for syncope. Patients should be cautioned about driving, operating machinery, or performing hazardous tasks when initiating therapy [*see Adverse Reactions and Use in Specific Populations*].

Renal Impairment

In a clinical pharmacology study, plasma concentrations (AUC and C_{max}) of silodosin were approximately three times higher in subjects with moderate renal impairment compared with subjects with normal renal function, while half-lives of silodosin doubled in duration. The dose of RAPAFLO should be reduced to 4 mg in patients with moderate renal impairment. Exercise caution and monitor such patients for adverse events [*see Use in Specific Populations*].

RAPAFLO is contraindicated in patients with severe renal impairment [*see Contraindications*].

Hepatic Impairment

RAPAFLO has not been tested in patients with severe hepatic impairment, and therefore, should not be prescribed to such patients [*see Contraindications and Use in Specific Populations*].

Pharmacokinetic Drug-Drug Interactions

In a drug interaction study, co-administration of a single 8 mg dose of RAPAFLO with 400 mg ketoconazole, a strong CYP3A4 inhibitor, caused a 3.8-fold increase in maximum plasma silodosin concentrations and 3.2-fold increase in silodosin exposure (i.e., AUC). Concomitant use of ketoconazole or other strong CYP3A4 inhibitors (e.g., itraconazole, clarithromycin, ritonavir) is therefore contraindicated [*see Drug Interactions*].

Pharmacodynamic Drug-Drug Interactions

The pharmacodynamic interactions between silodosin and other alpha-blockers have not been determined. However, interactions may be expected, and RAPAFLO should not be used in combination with other alpha-blockers [*see Drug Interactions*].

A specific pharmacodynamic interaction study between silodosin and antihypertensive agents has not been performed. However, patients in the Phase 3 clinical studies taking concomitant antihypertensive medications with RAPAFLO did not experience a significant increase in the incidence of syncope, dizziness, or orthostasis. Nevertheless, exercise caution during concomitant use with antihypertensives and monitor patients for possible adverse events [*see Adverse Reactions and Drug Interactions*].

Caution is also advised when alpha-adrenergic blocking agents including RAPAFLO are co-administered with PDE5 inhibitors. Alpha-adrenergic blockers and PDE5 inhibitors are both vasodilators that can lower blood pressure. Concomitant use of these two drug classes can potentially cause symptomatic hypotension [*see Drug Interactions*].

Carcinoma of the Prostate

Carcinoma of the prostate and BPH cause many of the same symptoms. These two diseases frequently co-exist. Therefore, patients thought to have BPH should be examined prior to starting therapy with RAPAFLO to rule out the presence of carcinoma of the prostate.

Intraoperative Floppy Iris Syndrome

Intraoperative Floppy Iris Syndrome has been observed during cataract surgery in some patients on alpha-1 blockers or previously treated with alpha-1 blockers. This variant of small pupil syndrome is characterized by the combination of a flaccid iris that billows in response to intraoperative irrigation currents; progressive intraoperative miosis despite preoperative dilation with standard mydriatic drugs; and potential prolapse of the iris toward the phacoemulsification incisions. Patients planning cataract surgery should be told to inform their ophthalmologist that they are taking RAPAFLO [*see Adverse Reactions*].

Laboratory Test Interactions

No laboratory test interactions were observed during clinical evaluations. Treatment with RAPAFLO for up to 52 weeks had no significant effect on prostate-specific antigen (PSA).

ADVERSE REACTIONS

Clinical Trials Experience

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

In U.S. clinical trials, 897 patients with BPH were exposed to 8 mg RAPAFLO daily. This includes 486 patients exposed for 6 months and 168 patients exposed for 1 year. The population was 44 to 87 years of age, and predominantly Caucasian. Of these patients, 42.8% were 65 years of age or older and 10.7% were 75 years of age or older.

In double-blind, placebo controlled, 12-week clinical trials, 466 patients were administered RAPAFLO and 457 patients were administered placebo. At least one treatment-emergent adverse reaction was reported by 55.2% of RAPAFLO treated patients (36.8% for placebo treated). The majority (72.1%) of adverse reactions for the RAPAFLO treated patients (59.8% for placebo treated) were qualified by the investigator as mild. A total of 6.4% of RAPAFLO treated patients (2.2% for placebo treated) discontinued therapy due to an adverse reaction (treatment-emergent), the most common reaction being retrograde ejaculation (2.8%) for RAPAFLO treated patients. Retrograde ejaculation is reversible upon discontinuation of treatment.

Adverse Reactions observed in at least 2% of patients:

The incidence of treatment-emergent adverse reactions listed in the following table were derived from two 12-week, multicenter, double-blind, placebo-controlled clinical studies of RAPAFLO 8 mg daily in BPH patients. Adverse reactions that occurred in at least 2% of patients treated with RAPAFLO and more frequently than with placebo are shown in Table 1.

Table 1 Adverse Reactions Occurring in ≥ 2% of Patients in 12-week, Placebo-Controlled Clinical Trials

Adverse Reactions	RAPAFLO N = 466 n (%)	Placebo N = 457 n (%)
Retrograde Ejaculation	131 (28.1)	4 (0.9)
Dizziness	15 (3.2)	5 (1.1)
Diarrhea	12 (2.6)	6 (1.3)
Orthostatic Hypotension	12 (2.6)	7 (1.5)
Headache	11 (2.4)	4 (0.9)
Nasopharyngitis	11 (2.4)	10 (2.2)
Nasal Congestion	10 (2.1)	1 (0.2)

In the two 12-week, placebo-controlled clinical trials, the following adverse events were reported by between 1% and 2% of patients receiving RAPAFLO and occurred more frequently than with placebo: insomnia, PSA increased, sinusitis, abdominal pain, asthenia, and rhinorrhea. One case of syncope in a patient taking prazosin concomitantly and one case of priapism were reported in the RAPAFLO treatment group.

In a 9-month open-label safety study of RAPAFLO, one case of Intraoperative Floppy Iris Syndrome (IFIS) was reported.

Postmarketing Experience

The following adverse reactions have been identified during post approval use of silodosin. 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:

Skin and subcutaneous tissue disorders: *toxic skin eruption, purpura*

Hepatobiliary disorders: *jaundice, impaired hepatic function associated with increased transaminase values*

DRUG INTERACTIONS

Moderate and Strong CYP3A4 Inhibitors

In a clinical metabolic inhibition study, a 3.8-fold increase in silodosin maximum plasma concentrations and 3.2-fold increase in silodosin exposure were observed with concurrent administration of a strong CYP3A4 inhibitor, 400 mg ketoconazole. Use of strong CYP3A4 inhibitors such as itraconazole or ritonavir may cause plasma concentrations of silodosin to increase. Concomitant administration of strong CYP3A4 inhibitors and RAPAFLO is contraindicated [*see Contraindications and Warnings and Precautions*].

The effect of moderate CYP3A4 inhibitors on the pharmacokinetics of silodosin has not been evaluated. Concomitant administration with moderate CYP3A4 inhibitors (e.g., diltiazem, erythromycin, verapamil) may increase concentration of RAPAFLO. Exercise caution and monitor patients for adverse events when co-administering RAPAFLO with moderate CYP3A4 inhibitors.

Strong P-glycoprotein (P-gp) Inhibitors

In vitro studies indicated that silodosin is a P-gp substrate. Ketoconazole, a CYP3A4 inhibitor that also inhibits P-gp, caused significant increase in exposure to silodosin. Inhibition of P-gp may lead to increased silodosin concentration. RAPAFLO is therefore not recommended in patients taking strong P-gp inhibitors such as cyclosporine.

Alpha-Blockers

The pharmacodynamic interactions between silodosin and other alpha-blockers have not been determined. However, interactions may be expected, and RAPAFLO should not be used in combination with other alpha-blockers [*see Warnings and Precautions*].

Digoxin

The effect of co-administration of RAPAFLO and digoxin 0.25 mg/day for 7 days was evaluated in a clinical trial in 16 healthy males, aged 18 to 45 years. Concomitant administration of RAPAFLO and digoxin did not significantly alter the steady state pharmacokinetics of digoxin. No dose adjustment is required.

PDE5 Inhibitors

Co-administration of RAPAFLO with a single dose of 100 mg sildenafil or 20 mg tadalafil was evaluated in a placebo-controlled clinical study that included 24 healthy male subjects, 45 to 78 years of age. Orthostatic vital signs were monitored in the 12-hour period following concomitant dosing. During this period, the total number of positive orthostatic test results was greater in the group receiving RAPAFLO plus a PDE5 inhibitor compared with RAPAFLO alone. No events of symptomatic orthostasis or dizziness were reported in subjects receiving RAPAFLO with a PDE5 inhibitor.

Other Concomitant Drug Therapy

Antihypertensives

The pharmacodynamic interactions between silodosin and antihypertensives have not been rigorously investigated in a clinical study. However, approximately one-third of the patients in clinical studies used concomitant antihypertensive medications with RAPAFLO. The incidence of dizziness and orthostatic hypotension in these patients was higher than in the general silodosin population (4.6% versus 3.8% and 3.4% versus 3.2%, respectively). Exercise caution during concomitant use with antihypertensives and monitor patients for possible adverse events [*see Warnings and Precautions*].

Metabolic Interactions

In vitro data indicate that silodosin does not have the potential to inhibit or induce cytochrome P450 enzyme systems.

Food Interactions

The effect of a moderate fat, moderate calorie meal on silodosin pharmacokinetics was variable and decreased silodosin maximum plasma concentration (C_{max}) by approximately 18 - 43% and exposure (AUC) by 4 - 49% across three different studies. Safety and efficacy clinical trials for RAPAFLO were always conducted in the presence of food intake. Patients should be instructed to take silodosin with a meal to reduce risk of adverse events.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category B. RAPAFLO is not indicated for use in women.

An embryo/fetal study in rabbits showed decreased maternal body weight at 200 mg/kg/day (approximately 13-25 times the maximum recommended human exposure or MRHE of silodosin via AUC). No statistically significant teratogenicity was observed at this dose.

Silodosin was not teratogenic when administered to pregnant rats during organogenesis at 1000 mg/kg/day (estimated to be approximately 20 times the MRHE). No maternal or fetal effects were observed at this dose. Rats and rabbits do not produce glucuronidated silodosin, which is present in human serum at approximately 4 times the level of circulating silodosin and which has similar pharmacological activity to silodosin.

No effects on physical or behavioral development of offspring were observed when rats were treated during pregnancy and lactation at up to 300 mg/kg/day.

Pediatric Use

RAPAFLO is not indicated for use in pediatric patients. Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

In double-blind, placebo-controlled, 12-week clinical studies of RAPAFLO, 259 (55.6%) were under 65 years of age, 207 (44.4%) patients were 65 years of age and over, while 60 (12.9%) patients were 75 years of age and over. Orthostatic hypotension was reported in 2.3% of RAPAFLO patients < 65 years of age (1.2% for placebo), 2.9% of RAPAFLO patients ≥ 65 years of age (1.9% for placebo), and 5.0% of patients ≥ 75 years of age (0% for placebo). There were otherwise no significant differences in safety or effectiveness between older and younger patients.

Renal Impairment

The effect of renal impairment on silodosin pharmacokinetics was evaluated in a single dose study of six male patients with moderate renal impairment and seven male subjects with normal renal function. Plasma concentrations of silodosin were approximately three times higher in subjects with moderate renal impairment compared with subjects with normal renal function.

RAPAFLO should be reduced to 4 mg per day in patients with moderate renal impairment. Exercise caution and monitor patients for adverse events.

RAPAFLO has not been studied in patients with severe renal impairment. RAPAFLO is contraindicated in patients with severe renal impairment [*see Contraindications and Warnings and Precautions*].

Hepatic Impairment

In a study comparing nine male patients with moderate hepatic impairment (Child-Pugh scores 7 to 9), to nine healthy male subjects, the single dose pharmacokinetics of silodosin were not significantly altered in patients with hepatic impairment. No dosing adjustment is required in patients with mild or moderate hepatic impairment.

RAPAFLO has not been studied in patients with severe hepatic impairment. RAPAFLO is contraindicated in patients with severe hepatic impairment [*see Contraindications and Warnings and Precautions*].

OVERDOSAGE

RAPAFLO was evaluated at doses of up to 48 mg/day in healthy male subjects. The dose-limiting adverse event was postural hypotension.

Should overdose of RAPAFLO lead to hypotension, support of the cardiovascular system is of first importance. Restoration of blood pressure and normalization of heart rate may be accomplished by maintaining the patient in the supine position. If this measure is inadequate, administration of intravenous fluid should be considered. If necessary, vasopressors could be used, and renal function should be monitored and supported as needed. Dialysis is unlikely to be of significant benefit since silodosin is highly (97%) protein bound.

Watson®

Manufactured by: Watson Laboratories, Inc., Corona, CA 92880 USA
Distributed by: Watson Pharma, Inc., Parsippany, NJ 07054 USA
Under license from: Kissei Pharmaceutical Co., Ltd., Nagano, Japan
For all medical inquiries contact: WATSON Medical Communications, Parsippany, NJ 07054
800-272-5525
For additional information see:
www.rapaflo.com
or call 1-866-RAPAFLO (727-2356)

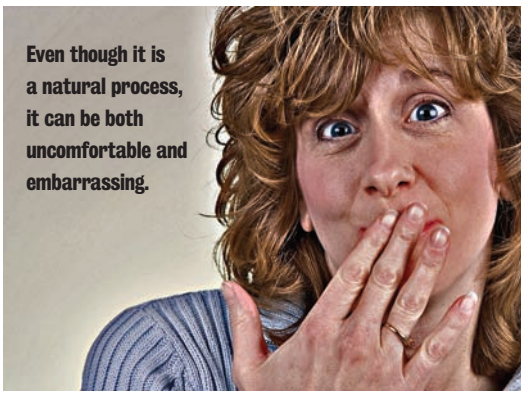
Rx Only Revised: November 2011 173761-3

THE INS AND OUTS OF

Intestinal Gas

Belching, bloating and flatulence... everyone experiences them to some extent. When it interferes with daily living, it's time to get some help.

It's a fact of life. The intestinal tract generates gas as a normal part of the digestive process. In fact, the average healthy person will produce about 1 to 4 pints of it a day and, whether they notice it or not, pass gas between 14 and 25 times. But even though it is a natural process, it can be both uncomfortable and embarrassing, especially in periods when variations in diet or intestinal upset lead to a temporary increase in gas production.



Even though it is a natural process, it can be both uncomfortable and embarrassing.

There are two main sources for what becomes intestinal gas: swallowed air and the breakdown of certain undigested foods by the bacteria naturally present in the colon.

Small amounts of air are swallowed in the normal course of eating and drinking, especially if you're talking at the same time. Some people, however, do more than the usual amount of air swallowing (known as aerophagia) as a result of eating very fast, chewing gum, smoking, drinking through a straw, and even from wearing loose dentures.

"It's normal to belch after having a big meal or drinking soda," says Dr. Arif Muslim of the GI Division, "because gas which you have swallowed comes back up. But some patients come to us complaining that they continuously burp." Once upper GI problems, such as GERD or peptic ulcers are ruled out, "the likelihood is it is something of a psychological problem," says Dr. Muslim.

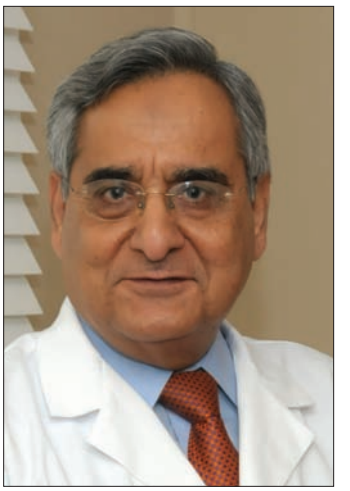
At one time these "chronic belchers" discovered that burping relieved gastric discomfort, and the practice unknowingly became a habit. "Such patients," says Muslim, "often swallow air, hold it in the esophagus, then burp it back. Treatment involves helping them understand what's going on and developing a way to change the behavior."

Abdominal bloating is a more complex issue and a wider range of processes can contribute to it. "Bloating," says Dr. Muslim, "can be a result of aerophagia, it can be diet-related, and it can also be a symptom of irritable bowel disease or any condition, such as Crohn's disease, that causes intestinal inflammation or obstruction." In disease states, the sense of bloating is not actually the result of increased gas, it is a heightened sensitivity to normal quantities of gas.

According to Dr. Muslim, the most common foods that cause bloating are milk products. "A large proportion of the population is lactose intolerant," says Muslim. "Milk products go into the small intestines where they should be broken down into glucose and galactose, two sugars, and absorbed. The process requires an enzyme called lactase. As we grow older, we tend to lose sufficient production of that enzyme. Without lactase, the sugars don't get absorbed but pass into the colon, where bacteria ferments them. The result is gas, which is passed from below." If testing shows lactose intolerance is the cause, treatment is reasonably simple: avoid milk products or take lactase in an artificial form.

"There are a number of foods that I call flatogenic, that is, they produce a lot of gas," Muslim says. "These include beans, vegetables in the brassica family (cabbage, broccoli, etc.), sorbitol (the sweetener in sugar-free gums), and starches." These make their way to the large intestine where, fermented by bacteria, they produce gas, which is eventually passed through the rectum.

Diet, life-style changes, enzymes, and medication can make a big difference in a person's experience of intestinal gas. The physicians in the GI Division can help devise a personalized program to improve your situation.



Arif M. Muslim, MD

"Mankind has been curious about intestinal gas since at least the days of Hippocrates, who published the first medical paper on the subject. In 400 BC he wrote, "Passing gas is necessary to well-being." And, of course, he was correct.

Everyone has gas in his or her digestive system and everyone needs to eliminate it. Probably half the patients in a GI office have some complaint related to gas. They may be concerned with belching, which is upper gas; bloating or abdominal distention, which is in the midsection; and the third thing they complain about is passing gas from below, flatulence.

Patients are sometimes embarrassed to talk about it, but the older they get and the more trouble they're in, the more likely they are to come in and ask for help.

The most common symptoms of gas—belching, flatulence, bloating, and abdominal pain—are, in some instances, the signs of organic intestinal disorders, such as irritable bowel syndrome. Most of the time, however, it's just gas. And frequently, the problem can be addressed with dietary and lifestyle changes, an understanding of the digestive tract, and a little medicine."

WHAT YOU NEED TO KNOW ABOUT

Crohn's Disease

Though there is no cure for this challenging disease, success can be measured in years of symptom-free, high-quality living.

Crohn's disease is a very challenging condition to treat," says Dr. Sunil Khurana. In the 80 years since Dr. Burrill B. Crohn described it in a medical paper, neither its precise cause nor a cure for it has been discovered.

Crohn's disease (CD) is a chronic inf ammatory disorder of the digestive tract. It most commonly affects the lower part of the small intestine and colon but can involve any area of the tract. In most people, it is diagnosed at an early age, between 15 and 35. Because its symptoms are similar to those of ulcerative colitis, another inf ammatory bowel disease, and to other intestinal disorders, an extensive series of tests may be needed to arrive at a definitive diagnosis and to discover how much of the GI tract has been affected.

The main goal of treatment has traditionally been seen as controlling the inf ammation as a means to relieving the major symptoms—such as abdominal pain, diarrhea, and rectal bleeding—and avoiding long-term complications, which can include the need for surgery. The particulars of the therapies employed depend on the location and severity of the disease and the individual's response to the various medicines that are available.

As there is no cure, success is measured by control of inf ammation and symptoms, and by the ability of therapy to invoke periods of remission. People with Crohn's disease may be free of symptoms for years at a time, but "f are-ups" and recurrence of symptoms almost invariably occur.

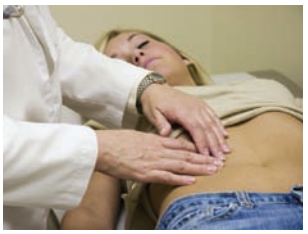
Things are better now

In earlier years, physicians focused heavily on symptom relief. "Now, there is enough data that shows that healing is the way to go," says Dr. Khurana. "If the ulcers and the mucosal inf ammation characterizing CD heals, the patient's prognosis is much better."

Several categories of drugs, using different mechanisms to control inf ammation, have been available for some time. None are effective for every patient, and each has its own side effects and limitations, so the proper drug regimen is arrived at gradually.

In recent years, a new type of drug, called biologicals, has been approved for use in CD. Biologicals are proteins engineered to inhibit components of the immune system that play a role in inf ammation.

In most people, Crohn's disease is diagnosed at an early age, between 15 and 35.



In Dr. Khurana's view, "physicians have to be aggressive enough to use biological agents early. You don't fuss around for a year or two with older medications and use biologicals only as a last-line drug. You need to bring them on pretty early in the treatment. You can really change the course of the disease with these drugs and you can save some people from surgery.

"Things are demonstrably better now for people with Crohn's disease," says Khurana. "At one time it was often necessary for Crohn's patients to be hospitalized following a f are-up or acute episode. With today's newer medicines and treatment approaches, the need for many such hospitalizations is no longer there."

Premier's GI Division is now able to handle most people with CD as outpatients. It operates an infusion center where patients can receive regular infusions of crucial drugs like Remicade. "It's convenient for patients," says Khurana. "They don't have to go to the hospital; they become familiar with the staff; see the same faces all the time… it's like a social visit."

Khurana is confident that Premier is able to give its GI patients the best treatment available. "Because we've been involved in multiple clinical studies of newer drugs, we are often able to offer treatment to patients who have not responded to established drugs or other protocols."

Sunil K. Khurana, MD, FACG

"Crohn's normally starts pretty young. I have dozens of patients who were diagnosed between age 14 and 17. These are kids, they're not mature, and they have a very serious disease.

Management is two-phased. It's not only about good medical therapy. You need a lot more compassion than you might with adults. These kids should be on the soccer or baseball field, and they can't be. It's very difficult for them.

One of the things doctors need to do is spend a lot of time with these people. Not only talking about taking pills, but also understanding their underlying emotional state and giving them support. Talking to the family is equally important, especially the moms. They're so concerned that their kids are missing school, or not doing well, or are unable to participate in events.

I really believe you need a unique temperament to treat Crohn's disease; it's not something that should be handled by every GI. You need to take time, especially when you diagnose a patient early on or when you change his therapy. You may not see them in the office, but you talk to them on the phone for 15 or 20 minutes every day. You have to take care of each of them as a person, not as a disease."

- In a maintenance trial, of the patients who achieved clinical response at week 4, greater proportions of HUMIRA-treated patients, compared to placebo patients, were in clinical remission at week 26 (40% vs 17%, $P<0.001$) and week 56 (36% vs 12%, $P<0.001$)[1]
- HUMIRA can be self-injected at home or almost anywhere, after a physician determines that it is appropriate and after proper training in injection technique. Instruct patients to refer to storage instructions found in the Medication Guide[1]

Indications[1]

HUMIRA is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. HUMIRA is indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.

Safety Considerations[1]

Serious Infections

Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death. These infections include active tuberculosis (TB), reactivation of latent TB, invasive fungal infections, and bacterial, viral, and other infections due to opportunistic pathogens. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Malignancies

Lymphoma, including a rare type of T-cell lymphoma, and other malignancies, some fatal, have been reported in patients treated with TNF blockers, including HUMIRA.

Other Serious Adverse Reactions

Patients treated with HUMIRA also may be at risk for other serious adverse reactions, including anaphylaxis, hepatitis B virus reactivation, demyelinating disease, cytopenias, pancytopenia, heart failure, and a lupus-like syndrome.

HUMIRA®
adalimumab

IMPORTANT SAFETY INFORMATION[1]

SERIOUS INFECTIONS

Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

HUMIRA should be discontinued if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before HUMIRA use and during therapy. Treatment for latent TB should be initiated prior to HUMIRA use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.**

The risks and benefits of treatment with HUMIRA should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with HUMIRA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

- Do not start HUMIRA in patients with an active infection, including localized infections.
- Patients older than 65 years, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants may be at greater risk of infection.
- Exercise caution in patients with chronic or recurrent infection or with underlying conditions which may predispose them to infection, patients who have been exposed to TB, patients with a history of opportunistic infection, or patients who have resided or traveled in regions where TB or mycoses are endemic.
- Patients who develop a new infection should undergo a prompt and complete diagnostic workup, and appropriate antimicrobial therapy should be initiated.
- Drug interactions with biologic products: Concurrent use of anakinra or abatacept with HUMIRA is not recommended, as the combination of anakinra or abatacept with TNF blockers has been associated with an increased risk of serious infections. This risk has also been observed with rheumatoid arthritis patients treated with rituximab who received subsequent treatment with a TNF blocker.

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which HUMIRA is a member. Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including HUMIRA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases has occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants.

- The risks and benefits of HUMIRA treatment should be considered prior to initiating or continuing therapy in a patient with known malignancy.
- More cases of malignancies were observed among HUMIRA-treated patients compared to control patients in clinical trials.
- Non-melanoma skin cancer (NMSC) has been reported during clinical trials for HUMIRA-treated patients. All patients, particularly those with history of prolonged immunosuppressant or PUVA therapy, should be examined for the presence of NMSC prior to and during treatment with HUMIRA.
- In HUMIRA clinical trials, there was an approximate 3-fold higher rate of lymphoma than expected in the general U.S. population. Patients with chronic inflammatory diseases, particularly with highly active disease and/or chronic exposure to immunosuppressant therapies, may be at higher risk of lymphoma than the general population, even in the absence of TNF blockers.
- Postmarketing cases of acute and chronic leukemia were reported with TNF blocker use.
- Approximately half of the postmarketing cases of malignancies in children, adolescents, and young adults receiving TNF blockers were lymphomas; other cases included rare malignancies associated with immunosuppression and malignancies not usually observed in children and adolescents.

HYPERSENSITIVITY

- Anaphylaxis and angioneurotic edema have been reported rarely following HUMIRA administration.
- If a serious allergic reaction occurs, stop HUMIRA and institute appropriate therapy.

HEPATITIS B VIRUS REACTIVATION

- Use of TNF blockers, including HUMIRA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases have been fatal.
- Patients at risk for HBV infection should be evaluated for prior evidence of HBV infection before initiating TNF blocker therapy.
- Exercise caution in patients who are carriers of HBV and monitor them during and after treatment with HUMIRA.
- Discontinue HUMIRA and begin antiviral therapy in patients who develop HBV reactivation.
- Exercise caution when considering resumption of HUMIRA therapy after appropriate treatment for HBV.

NEUROLOGIC REACTIONS

- TNF blockers, including HUMIRA, have been associated in rare cases with new onset or exacerbation of central nervous system and peripheral demyelinating diseases, including multiple sclerosis, optic neuritis, and Guillain-Barré syndrome.
- Exercise caution when considering HUMIRA for patients with these disorders.

HEMATOLOGIC REACTIONS

- Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia (e.g. thrombocytopenia, leukopenia) has been infrequently reported with HUMIRA.
- Consider stopping HUMIRA in patients with significant hematologic abnormalities.

CONGESTIVE HEART FAILURE

- Worsening or new onset congestive heart failure (CHF) may occur.
- Exercise caution in patients with CHF and monitor them carefully.

AUTOIMMUNITY

- Treatment with HUMIRA may result in the formation of autoantibodies and, rarely, in development of a lupus-like syndrome.
- Discontinue treatment if symptoms of a lupus-like syndrome develop.

IMMUNIZATIONS

- Patients on HUMIRA should not receive live vaccines.
- It is recommended that juvenile idiopathic arthritis patients, if possible, be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating HUMIRA therapy.

ADVERSE REACTIONS

- The most common adverse reactions in HUMIRA clinical trials (incidence >10%) were: infections (e.g. upper respiratory, sinusitis), injection site reactions, headache, and rash.

Please see Brief Summary of full Prescribing Information on following pages.

Reference: 1. HUMIRA Injection [package insert]. North Chicago, IL: Abbott Laboratories.

HUMIRA®
adalimumab

Abbott
A Promise for Life

HUMIRA® (adalimumab)

PROFESSIONAL BRIEF SUMMARY
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

WARNINGS: SERIOUS INFECTIONS AND MALIGNANCY

SERIOUS INFECTIONS

Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death *[see Warnings and Precautions]*. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

HUMIRA should be discontinued if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before HUMIRA use and during therapy. Treatment for latent TB should be initiated prior to HUMIRA use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.**

The risks and benefits of treatment with HUMIRA should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with HUMIRA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy. *[See Warnings and Precautions and Adverse Reactions]*

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which HUMIRA is a member. *[See Warnings and Precautions]* Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including HUMIRA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases has occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants.

INDICATIONS AND USAGE

Rheumatoid Arthritis

HUMIRA is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. HUMIRA can be used alone or in combination with methotrexate or other non-biologic disease-modifying anti-rheumatic drugs (DMARDs).

Juvenile Idiopathic Arthritis

HUMIRA is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 4 years of age and older. HUMIRA can be used alone or in combination with methotrexate.

Psoriatic Arthritis

HUMIRA is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis. HUMIRA can be used alone or in combination with non-biologic DMARDs.

Ankylosing Spondylitis

HUMIRA is indicated for reducing signs and symptoms in adult patients with active ankylosing spondylitis.

Crohn's Disease

HUMIRA is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. HUMIRA is indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.

Plaque Psoriasis

HUMIRA is indicated for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate. HUMIRA should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician *[see Boxed Warnings and Warnings and Precautions]*.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

(see also Boxed WARNINGS)

Serious Infections

Patients treated with HUMIRA are at increased risk for developing serious infections involving various organ systems and sites that may lead to hospitalization or death. Opportunistic infections due to bacterial, mycobacterial, invasive fungal, viral, parasitic, or other opportunistic pathogens including aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, legionellosis, listeriosis, pneumocystosis and tuberculosis have been reported with TNF blockers. Patients have frequently presented with disseminated rather than localized disease.

The concomitant use of a TNF blocker and abatacept or anakinra was associated with a higher risk of serious infections in patients with rheumatoid arthritis (RA); therefore, the concomitant use of HUMIRA and these biologic products is not recommended in the treatment of patients with RA [*see Warnings and Precautions and Drug Interactions*].

Treatment with HUMIRA should not be initiated in patients with an active infection, including localized infections. Patients greater than 65 years of age, patients with co-morbid conditions and/or patients taking concomitant immunosuppressants (such as corticosteroids or methotrexate), may be at greater risk of infection. The risks and benefits of treatment should be considered prior to initiating therapy in patients:

- with chronic or recurrent infection;
- who have been exposed to tuberculosis;
- with a history of an opportunistic infection;
- who have resided or traveled in areas of endemic tuberculosis or endemic mycoses, such as histoplasmosis, coccidioidomycosis, or blastomycosis; or
- with underlying conditions that may predispose them to infection.

Tuberculosis

Cases of reactivation of tuberculosis or new tuberculosis infections have been observed in patients receiving HUMIRA, including patients who have previously received treatment for latent or active tuberculosis. Patients should be evaluated for tuberculosis risk factors and tested for latent infection prior to initiating HUMIRA and periodically during therapy.

Treatment of latent tuberculosis infection prior to therapy with TNF blocking agents has been shown to reduce the risk of tuberculosis reactivation during therapy.

Anti-tuberculosis therapy should also be considered prior to initiation of HUMIRA in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent tuberculosis but having risk factors for tuberculosis infection. Consultation with a physician with expertise in the treatment of tuberculosis is recommended to aid in the decision whether initiating anti-tuberculosis therapy is appropriate for an individual patient.

Tuberculosis should be strongly considered in patients who develop a new infection during HUMIRA treatment, especially in patients who have previously or recently traveled to countries with a high prevalence of tuberculosis, or who have had close contact with a person with active tuberculosis.

Monitoring

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with HUMIRA, including the development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy. Tests for latent tuberculosis infection may also be falsely negative while on therapy with HUMIRA.

HUMIRA should be discontinued if a patient develops a serious infection or sepsis. A patient who develops a new infection during treatment with HUMIRA should be closely monitored, undergo a prompt and complete diagnostic workup appropriate for an immunocompromised patient, and appropriate antimicrobial therapy should be initiated.

Invasive Fungal Infections

For patients who reside or travel in regions where mycoses are endemic, invasive fungal infection should be suspected if they develop a serious systemic illness. Appropriate empiric antifungal therapy should be considered while a diagnostic workup is being performed. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. When feasible, the decision to administer empiric antifungal therapy in these patients should be made in consultation with a physician with expertise in the diagnosis and treatment of invasive fungal infections and should take into account both the risk for severe fungal infection and the risks of antifungal therapy.

Malignancies

The risks and benefits of TNF-blocker treatment including HUMIRA should be considered prior to initiating therapy in patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing a TNF blocker in patients who develop a malignancy.

Malignancies in Adults

In the controlled portions of clinical trials of some TNF-blockers, including HUMIRA, more cases of malignancies have been observed among TNF-blocker-treated adult patients compared to control-treated adult patients. During the controlled portions of 32 global HUMIRA clinical trials in adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), and plaque psoriasis (Ps), malignancies, other than non-melanoma (basal cell and squamous cell) skin cancer, were observed at a rate (95% confidence interval) of 0.6 (0.38, 0.93) per 100 patient-years among 6694 HUMIRA-treated patients versus a rate of 0.5 (0.28, 1.05) per 100 patient-years among 3749 control-treated patients (median duration of treatment of 4 months for HUMIRA-treated patients and 4 months for control-treated patients). In 45 global controlled and uncontrolled clinical trials of HUMIRA in adult patients with RA, PsA, AS, CD and Ps, the most frequently observed malignancies, other than lymphoma and NMSC, were breast, colon, prostate, lung, and melanoma. The malignancies in HUMIRA-treated patients in the controlled and uncontrolled portions of the studies were similar in type and number to what would be expected in the general U.S. population according to the SEER database (adjusted for age, gender, and race).

In controlled trials of other TNF blockers in adult patients at higher risk for malignancies (i.e., patients with COPD with a significant smoking history and cyclophosphamide-treated patients with Wegener's granulomatosis), a greater portion of malignancies occurred in the TNF blocker group compared to the control group.

Non-Melanoma Skin Cancer

During the controlled portions of 32 global HUMIRA clinical trials in adult patients with RA, PsA, AS, CD, and Ps, the rate (95% confidence interval) of NMSC was 0.7 (0.50, 1.11) per 100 patient-years among HUMIRA-treated patients and 0.2 (0.06, 0.56) per 100 patient-years among control-treated patients. All patients, and in particular patients with a medical history of prior prolonged immunosuppressant therapy or psoriasis patients with a history of PUVA treatment should be examined for the presence of NMSC prior to and during treatment with HUMIRA.

Lymphoma and Leukemia

In the controlled portions of clinical trials of all the TNF-blockers in adults, more cases of lymphoma have been observed among TNF blocker-treated patients compared to control-treated patients. In the controlled portions of 32 global HUMIRA clinical trials in adult patients with RA, PsA, AS, CD, and Ps, 3 lymphomas occurred among 6694 HUMIRA-treated patients versus 1 among 3749 control-treated patients. In 45 global controlled and uncontrolled clinical trials of HUMIRA in adult patients with RA, PsA, AS, CD and Ps with a median duration of approximately 0.6 years, including 22,026 patients and over 32,000 patient-years of HUMIRA, the observed rate of lymphomas was approximately 0.11 per 100 patient-years. This is approximately 3-fold higher than expected in the general U.S. population according to the SEER database (adjusted for age, gender, and race). Rates of lymphoma in clinical trials of HUMIRA cannot be compared to rates of lymphoma in clinical trials of other TNF blockers and may not predict the rates observed in a broader patient population. Patients with RA and other chronic inflammatory diseases, particularly those with highly active disease and/or chronic exposure to immunosuppressant therapies, may be at a higher risk (up to several fold) than the general population for the development of lymphoma, even in the absence of TNF blockers. Post-marketing cases of acute and chronic leukemia have been reported in association with TNF-blocker use in RA and other indications. Even in the absence of TNF-blocker therapy, patients with RA may be at a higher risk (approximately 2-fold) than the general population for the development of leukemia.

Malignancies in Pediatric Patients and Young Adults

Malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blockers (initiation of therapy ≤ 18 years of age), of which HUMIRA is a member. Approximately half the cases were lymphomas, including Hodgkin's and non-Hodgkin's lymphoma. The other cases represented a variety of different malignancies and included rare malignancies usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents. The malignancies occurred after a median of 30 months of therapy (range 1 to 84 months). Most of the patients were receiving concomitant immunosuppressants. These cases were reported post-marketing and are derived from a variety of sources including registries and spontaneous postmarketing reports.

Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including HUMIRA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases has occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all of these patients had received treatment with the immunosuppressants azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants.

Hypersensitivity Reactions

In postmarketing experience, anaphylaxis and angioneurotic edema have been reported rarely following HUMIRA administration. If an anaphylactic or other serious allergic reaction occurs, administration of HUMIRA should be discontinued immediately and appropriate therapy instituted. In clinical trials of HUMIRA in adults, allergic reactions overall (e.g., allergic rash, anaphylactoid reaction, fixed drug reaction, non-specified drug reaction, urticaria) have been observed in approximately 1% of patients.

Hepatitis B Virus Reactivation

Use of TNF blockers, including HUMIRA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. In some instances, HBV reactivation occurring in conjunction with TNF blocker therapy has been fatal. The majority of these reports have occurred in patients concomitantly receiving other medications that suppress the immune system, which may also contribute to HBV reactivation. Patients at risk for HBV infection should be evaluated for prior evidence of HBV infection before initiating TNF blocker therapy. Prescribers should exercise caution in prescribing TNF blockers for patients identified as carriers of HBV. Adequate data are not available on the safety or efficacy of treating patients who are carriers of HBV with anti-viral therapy in conjunction with TNF blocker therapy to prevent HBV reactivation. In patients who develop HBV reactivation, HUMIRA should be stopped and effective anti-viral therapy with appropriate supportive treatment should be initiated. The safety of resuming TNF blocker therapy after HBV reactivation is controlled is not known.

Neurologic Reactions

Use of TNF blocking agents, including HUMIRA, has been associated with rare cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of central nervous system demyelinating disease, including multiple sclerosis (MS) and optic neuritis, and peripheral demyelinating disease, including Guillain-Barré syndrome. Prescribers should exercise caution in considering the use of HUMIRA in patients with preexisting or recent-onset central or peripheral nervous system demyelinating disorders.

Hematological Reactions

Rare reports of pancytopenia including aplastic anemia have been reported with TNF blocking agents. Adverse reactions of the hematologic system, including medically significant cytopenia (e.g., thrombocytopenia, leukopenia) have been infrequently reported with HUMIRA. The causal relationship of these reports to HUMIRA remains unclear. All patients should be advised to seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g., persistent fever, bruising, bleeding, pallor) while on HUMIRA. Discontinuation of HUMIRA therapy should be considered in patients with confirmed significant hematologic abnormalities.

Use with Anakinra

Concurrent use of anakinra (an interleukin-1 antagonist) and another TNF-blocker, was associated with a greater proportion of serious infections and neutropenia and no added benefit compared with the TNF-blocker alone in patients with RA. Therefore, the combination of HUMIRA and anakinra is not recommended *[see Drug Interactions]*.

Heart Failure

Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF blockers. Cases of worsening CHF have also been observed with HUMIRA. Physicians should exercise caution when using HUMIRA in patients who have heart failure and monitor them carefully.

Autoimmunity

Treatment with HUMIRA may result in the formation of autoantibodies and, rarely, in the development of a lupus-like syndrome. If a patient develops symptoms suggestive of a lupus-like syndrome following treatment with HUMIRA, treatment should be discontinued *[see Adverse Reactions]*.

Immunizations

In a placebo-controlled clinical trial of patients with rheumatoid arthritis, no difference was detected in anti-pneumococcal antibody response between HUMIRA and placebo treatment groups when the pneumococcal polysaccharide vaccine and influenza vaccine were administered concurrently with HUMIRA. Patients on HUMIRA may receive concurrent vaccinations, except for live vaccines. No data are available on the secondary transmission of infection by live vaccines in patients receiving HUMIRA.

It is recommended that juvenile idiopathic arthritis patients, if possible, be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating HUMIRA therapy. Patients on HUMIRA may receive concurrent vaccinations, except for live vaccines.

Use with Abatacept

In controlled trials, the concurrent administration of TNF-blockers and abatacept was associated with a greater proportion of serious infections than the use of a TNF-blocker alone; the combination therapy, compared to the use of a TNF-blocker alone, has not demonstrated improved clinical benefit in the treatment of RA. Therefore, the combination of abatacept with TNF-blockers including HUMIRA is not recommended *[see Drug Interactions]*.

ADVERSE REACTIONS

Clinical Studies Experience

The most serious adverse reactions were:

- Serious Infections [*see Warnings and Precautions*]
- Malignancies [*see Warnings and Precautions*]

The most common adverse reaction with HUMIRA was injection site reactions. In placebo-controlled trials, 20% of patients treated with HUMIRA developed injection site reactions (erythema and/or itching, hemorrhage, pain or swelling), compared to 14% of patients receiving placebo. Most injection site reactions were described as mild and generally did not necessitate drug discontinuation.

The proportion of patients who discontinued treatment due to adverse reactions during the double-blind, placebo-controlled portion of Studies RA-I, RA-II, RA-III and RA-IV was 7% for patients taking HUMIRA and 4% for placebo-treated patients. The most common adverse reactions leading to discontinuation of HUMIRA were clinical flare reaction (0.7%), rash (0.3%) and pneumonia (0.3%).

Infections

In the controlled portions of the 32 global HUMIRA clinical trials in adult patients with RA, PsA, AS, CD and Ps, the rate of serious infections was 4.7 per 100 patient-years in 6694 HUMIRA-treated patients versus a rate of 2.7 per 100 patient-years in 3749 control-treated patients. Serious infections observed included pneumonia, septic arthritis, prosthetic and post-surgical infections, erysipelas, cellulitis, diverticulitis, and pyelonephritis *[see Warnings and Precautions]*.

Tuberculosis and Opportunistic Infections

In 45 global controlled and uncontrolled clinical trials in RA, PsA, AS, CD and Ps that included 22,026 HUMIRA-treated patients, the rate of reported active tuberculosis was 0.22 per 100 patient-years and the rate of positive PPD conversion was 0.07 per 100 patient-years. In a subgroup of 8940 U.S. and Canadian HUMIRA-treated patients, the rate of reported active TB was 0.07 per 100 patient-years and the rate of positive PPD conversion was 0.06 per 100 patient-years. These trials included reports of miliary, lymphatic, peritoneal, and pulmonary TB. Most of the TB cases occurred within the first eight months after initiation of therapy and may reflect recrudescence of latent disease. In these global clinical trials, cases of serious opportunistic infections have been reported at an overall rate of 0.07 per 100 patient-years. Some cases of serious opportunistic infections and TB have been fatal *[see Warnings and Precautions]*.

Autoantibodies

In the rheumatoid arthritis controlled trials, 12% of patients treated with HUMIRA and 7% of placebo-treated patients that had negative baseline ANA titers developed positive titers at week 24. Two patients out of 3046 treated with HUMIRA developed clinical signs suggestive of new-onset lupus-like syndrome. The patients improved following discontinuation of therapy. No patients developed lupus nephritis or central nervous system symptoms. The impact of long-term treatment with HUMIRA on the development of autoimmune diseases is unknown.

Liver Enzyme Elevations

There have been reports of severe hepatic reactions including acute liver failure in patients receiving TNF-blockers. In controlled Phase 3 trials of HUMIRA (40 mg SC every other week) in patients with RA, PsA, and AS with control period duration ranging from 4 to 104 weeks, ALT elevations ≥ 3 x ULN occurred in 3.5% of HUMIRA-treated patients and 1.5% of control-treated patients. Since many of these patients in these trials were also taking medications that cause liver enzyme elevations (e.g., NSAIDS, MTX), the relationship between HUMIRA and the liver enzyme elevations is not clear. In controlled Phase 3 trials of HUMIRA (initial doses of 160 mg and 80 mg, or 80 mg and 40 mg on Days 1 and 15, respectively, followed by 40 mg every other week) in patients with Crohn's disease with control period duration ranging from 4 to 52 weeks, ALT elevations ≥ 3 x ULN occurred in 0.9% of HUMIRA-treated patients and 0.9% of control-treated patients. In controlled Phase 3 trials of HUMIRA (initial dose of 80 mg then 40 mg every other week) in patients with plaque psoriasis with control period duration ranging from 12 to 24 weeks, ALT elevations ≥ 3 x ULN occurred in 1.8% of HUMIRA-treated patients and 1.8% of control-treated patients.

Immunogenicity

Patients in Studies RA-I, RA-II, and RA-III were tested at multiple time points for antibodies to adalimumab during the 6- to 12-month period. Approximately 5% (58 of 1062) of adult rheumatoid arthritis patients receiving HUMIRA developed low-titer antibodies to adalimumab at least once during treatment, which were neutralizing *in vitro*. Patients treated with concomitant methotrexate had a lower rate of antibody development than patients on HUMIRA monotherapy (1% versus 12%). No apparent correlation of antibody development to adverse reactions was observed. With monotherapy, patients receiving every other week dosing may develop antibodies more frequently than those receiving weekly dosing. In patients receiving the recommended dosage of 40 mg every other week as monotherapy, the ACR 20 response was lower among antibody-positive patients than among antibody-negative patients. The long-term immunogenicity of HUMIRA is unknown. In patients with juvenile idiopathic arthritis, adalimumab antibodies were identified in 16% of HUMIRA-treated patients. In patients receiving concomitant methotrexate, the incidence was 6% compared to 26% with HUMIRA monotherapy.

In patients with ankylosing spondylitis, the rate of development of antibodies to adalimumab in HUMIRA-treated patients was comparable to patients with rheumatoid arthritis. In patients with psoriatic arthritis, the rate of antibody development in patients receiving HUMIRA monotherapy was comparable to patients with rheumatoid arthritis; however, in patients receiving concomitant methotrexate the rate was 7% compared to 1% in rheumatoid arthritis. In patients with Crohn's disease, the rate of antibody development was 3%. In patients with plaque psoriasis, the rate of antibody development with HUMIRA monotherapy was 8%. However, due to the limitation of the assay conditions, antibodies to adalimumab could be detected only when serum adalimumab levels were < 2 ug/ml. Among the patients whose serum adalimumab levels were < 2 ug/ml (approximately 40% of total patients studied), the immunogenicity rate was 20.7%. In plaque psoriasis patients who were on HUMIRA monotherapy and subsequently withdrawn from the treatment, the rate of antibodies to adalimumab after retreatment was similar to the rate observed prior to withdrawal.

Other Adverse Reactions

The data described below reflect exposure to HUMIRA in 2468 patients, including 2073 exposed for 6 months, 1497 exposed for greater than one year and 1380 in adequate and well-controlled studies (Studies RA-I, RA-II, RA-III, and RA-IV). HUMIRA was studied primarily in placebo-controlled trials and in long-term follow up studies for up to 36 months duration. The population had a mean age of 54 years, 77% were female, 91% were Caucasian and had moderately to severely active rheumatoid arthritis. Most patients received 40 mg HUMIRA every other week. Table 1 summarizes reactions reported at a rate of at least 5% in patients treated with HUMIRA 40 mg every other week compared to placebo and with an incidence higher than placebo. In Study RA-III, the types and frequencies of adverse reactions in the second year open-label extension were similar to those observed in the one-year double-blind portion.

Table 1. Adverse Reactions Reported by ≥5% of Patients Treated with HUMIRA During Placebo-Controlled Period of Rheumatoid Arthritis Studies

	HUMIRA 40 mg subcutaneous Every Other Week	Placebo
	(N=705)	(N=690)
Adverse Reaction (Preferred Term)		
Respiratory		
Upper respiratory infection	17%	13%
Sinusitis	11%	9%
Flu syndrome	7%	6%
Gastrointestinal		
Nausea	9%	8%
Abdominal pain	7%	4%
Laboratory Tests*		
Laboratory test abnormal	8%	7%
Hypercholesterolemia	6%	4%
Hyperlipidemia	7%	5%
Hematuria	5%	4%
Alkaline phosphatase increased	5%	3%
Other		
Headache	12%	8%
Rash	12%	6%
Accidental injury	10%	8%
Injection site reaction **	8%	1%
Back pain	6%	4%
Urinary tract infection	8%	5%
Hypertension	5%	3%

* Laboratory test abnormalities were reported as adverse reactions in European trials

** Does not include injection site erythema, itching, hemorrhage, pain or swelling

Juvenile Idiopathic Arthritis Clinical Studies

In general, the adverse reactions in the HUMIRA-treated pediatric patients in the juvenile idiopathic arthritis (JIA) trial were similar in frequency and type to those seen in adult patients *[see Warnings and Precautions, Adverse Reactions]*. Important findings and differences from adults are discussed in the following paragraphs.

HUMIRA was studied in 171 pediatric patients, 4 to 17 years of age, with polyarticular JIA. Severe adverse reactions reported in the study included neutropenia, streptococcal pharyngitis, increased aminotransferases, herpes zoster, myositis, metrorrhagia, appendicitis. Serious infections were observed in 4% of patients within approximately 2 years of initiation of treatment with HUMIRA and included cases of herpes simplex, pneumonia, urinary tract infection, pharyngitis, and herpes zoster.

A total of 45% of children experienced an infection while receiving HUMIRA with or without concomitant MTX in the first 16 weeks of treatment. The types of infections reported in HUMIRA-treated patients were generally similar to those commonly seen in JIA patients who are not treated with TNF blockers. Upon initiation of treatment, the most common adverse reactions occurring in the pediatric population treated with HUMIRA were injection site pain and injection site reaction (19% and 16%, respectively). A less commonly reported adverse event in children receiving HUMIRA was granuloma annulare which did not lead to discontinuation of HUMIRA treatment.

In the first 48 weeks of treatment, non-serious hypersensitivity reactions were seen in approximately 6% of children and included primarily localized allergic hypersensitivity reactions and allergic rash.

Isolated mild to moderate elevations of liver aminotransferases (ALT more common than AST) were observed in children with JIA exposed to HUMIRA alone; liver enzyme test elevations were more frequent among those treated with the combination of HUMIRA and MTX than those treated with HUMIRA alone. In general, these elevations did not lead to discontinuation of HUMIRA treatment.

In the JIA trial, 10% of patients treated with HUMIRA who had negative baseline anti-dsDNA antibodies developed positive titers after 48 weeks of treatment. No patient developed clinical signs of autoimmunity during the clinical trial.

Approximately 15% of children treated with HUMIRA developed mild-to-moderate elevations of creatine phosphokinase (CPK). Elevations exceeding 5 times the upper limit of normal were observed in several patients. CPK levels decreased or returned to normal in all patients. Most patients were able to continue HUMIRA without interruption.

Psoriatic Arthritis and Ankylosing Spondylitis Clinical Studies

HUMIRA has been studied in 395 patients with psoriatic arthritis (PsA) in two placebo-controlled trials and in an open label study and in 393 patients with ankylosing spondylitis (AS) in two placebo-controlled studies. The safety profile for patients with PsA and AS treated with HUMIRA 40 mg every other week was similar to the safety profile seen in patients with RA, HUMIRA Studies RA-I through IV.

Crohn's Disease Clinical Studies

HUMIRA has been studied in 1478 patients with Crohn's disease in four placebo-controlled and two open-label extension studies. The safety profile for patients with Crohn's disease treated with HUMIRA was similar to the safety profile seen in patients with RA.

Plaque Psoriasis Clinical Studies

HUMIRA has been studied in 1696 patients with plaque psoriasis in placebo-controlled and open-label extension studies. The safety profile for patients with plaque psoriasis treated with HUMIRA was similar to the safety profile seen in patients with RA with the following exceptions. In the placebo-controlled portions of the clinical trials in plaque psoriasis patients, HUMIRA-treated patients had a higher incidence of arthralgia when compared to controls (3% *vs.* 1%).

Postmarketing Experience

Adverse reactions have been reported during post-approval use of HUMIRA. 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 HUMIRA exposure.

Gastrointestinal disorders: Diverticulitis, large bowel perforations including perforations associated with diverticulitis and appendiceal perforations associated with appendicitis, pancreatitis

Respiratory disorders: Interstitial lung disease, including pulmonary fibrosis

Skin reactions: Stevens Johnson Syndrome, cutaneous vasculitis, erythema multiforme, new or worsening psoriasis (all sub-types including pustular and palmoplantar)

Vascular disorders: Systemic vasculitis

DRUG INTERACTIONS

Methotrexate

Although methotrexate (MTX) reduces the apparent adalimumab clearance, the data do not suggest the need for dose adjustment of either HUMIRA or MTX.

Biologic Products

In clinical studies in patients with RA, an increased risk of serious infections has been seen with the combination of TNF blockers with anakinra or abatacept, with no added benefit; therefore, use of HUMIRA with abatacept or anakinra is not recommended in patients with RA [*see Warnings and Precautions*]. A higher rate of serious infections has also been observed in patients with RA treated with rituximab who received subsequent treatment with a TNF blocker. There is insufficient information to provide recommendations regarding the concomitant use of HUMIRA and other biologic products for the treatment of RA, PsA, AS, Crohn's Disease, and plaque psoriasis.

Live Vaccines

Live vaccines should not be given concurrently with HUMIRA *[see Warnings and Precautions]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category B - There are no adequate and well-controlled studies in pregnant women. Because animal reproduction and developmental studies are not always predictive of human response, HUMIRA should be used during pregnancy only if clearly needed.

Pregnancy Registry: To monitor outcomes of pregnant women exposed to HUMIRA, a pregnancy registry has been established. Physicians are encouraged to register patients by calling 1-877-311-8972.

Nursing Mothers

It is not known whether adalimumab is excreted in human milk or absorbed systemically after ingestion. Because many drugs and immunoglobulins are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from HUMIRA, 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

Safety and efficacy of HUMIRA in pediatric patients for uses other than juvenile idiopathic arthritis (JIA) have not been established.

Juvenile Idiopathic Arthritis In the JIA trial, HUMIRA was shown to reduce signs and symptoms of active polyarticular JIA in patients 4 to 17 years of age. HUMIRA has not been studied in children less than 4 years of age, and there are limited data on HUMIRA treatment in children with weight <15 kg.

The safety of HUMIRA in pediatric patients in the JIA trial was generally similar to that observed in adults with certain exceptions *[see Adverse Reactions]*.

Post-marketing cases of malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blockers including HUMIRA *[see Warnings and Precautions]*.

Geriatric Use

A total of 519 rheumatoid arthritis patients 65 years of age and older, including 107 patients 75 years of age and older, received HUMIRA in clinical studies RA-I through IV. No overall difference in effectiveness was observed between these subjects and younger subjects. The frequency of serious infection and malignancy among HUMIRA treated subjects over 65 years of age was higher than for those under 65 years of age. Because there is a higher incidence of infections and malignancies in the elderly population in general, caution should be used when treating the elderly.

OVERDOSAGE

Doses up to 10 mg/kg have been administered to patients in clinical trials without evidence of dose-limiting toxicities. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment instituted immediately.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies of HUMIRA have not been conducted to evaluate the carcinogenic potential or its effect on fertility. No clastogenic or mutagenic effects of HUMIRA were observed in the *in vivo* mouse micronucleus test or the *Salmonella-Escherichia coli* (Ames) assay, respectively.

PATIENT COUNSELING INFORMATION

Patients or their caregivers should be provided the HUMIRA "Medication Guide" and provided an opportunity to read it and ask questions prior to initiation of therapy. The healthcare provider should ask the patient questions to determine any risk factors for treatment. Patients developing signs and symptoms of infection should seek medical evaluation immediately.

Patient Counseling

Patients should be advised of the potential benefits and risks of HUMIRA. Physicians should instruct their patients to read the Medication Guide before starting HUMIRA therapy and to reread each time the prescription is renewed.

- **Infections**
  Inform patients that HUMIRA may lower the ability of their immune system to fight infections. Instruct patients of the importance of contacting their doctor if they develop any symptoms of infection, including tuberculosis, invasive fungal infections, and reactivation of hepatitis B virus infections.
- **Malignancies**
  Patients should be counseled about the risk of malignancies while receiving HUMIRA.
- **Allergic Reactions**
  Patients should be advised to seek immediate medical attention if they experience any symptoms of severe allergic reactions. Advise latex-sensitive patients that the needle cap of the prefilled syringe contains latex.
- **Other Medical Conditions**
  Advise patients to report any signs of new or worsening medical conditions such as congestive heart failure, neurological disease, autoimmune disorders, or cytopenias. Advise patients to report any symptoms suggestive of a cytopenia such as bruising, bleeding, or persistent fever.

Revised: December, 2011
Ref: 03-A569-R27
Abbott Laboratories
North Chicago, IL 60064, U.S.A.
Master # 64C-758202

64E-760907

Abbott

PREMIER *medical group*
1 Columbia Street
Poughkeepsie, New York 12601
www.premiermedicalhv.com

RETURN SERVICE REQUESTED

Faces of Premier

Good healthcare requires teamwork. We're proud of the dedicated team that makes up Premier Medical Group. Their loyalty contributes to the comfort and security of our patients.

Laine Belmonte

Human Resources Manager

In March of this year, Premier Medical Group of the Hudson Valley appointed its first human resources manager. "It was time," says Dr. Evan Goldfischer, Premier's co-director. "We had grown to a point where we had about 140 employees and needed to have a dedicated HR person to make sure the employees are supported by a full-time professional."

That professional is Laine Belmonte.

"The challenge was attractive, since the department wasn't fully structured yet and the two divisions were not entirely integrated," says Belmonte. "I felt I could make a positive impact on building the infrastructure and establishing HR as a resource"

From the outset, Belmonte has been working on restructuring the health benefit offerings. "We're looking to make the benefits richer for the employees, while trying to contain costs for the organization," she says. Belmonte is also working closely with department supervisors on performance appraisals. "I help them deliver appropriate feedback to employees to keep them inspired, to help them understand what they're doing well and where they need to develop," Belmonte says.

Over the next several months, I will be working with our management team to revamp the performance appraisal process, refine our company policies and further develop our compensation strategy and structure.

"I like the caliber of the people I'm working with. There are a lot of knowledgeable, experienced people here," Belmonte says. "The spirit of what they want —to make employees happy, to make this a place where employees will stay for a long time—I think that's important. The happier our employees are, the more satisfied they will be in their jobs and the better care they will provide to our patients. Not every place cares about their employees as much as do both Dr. Goldfischer and Dr. Khurana. So perhaps the biggest focus of my job is to make sure our employees are content and stay content."