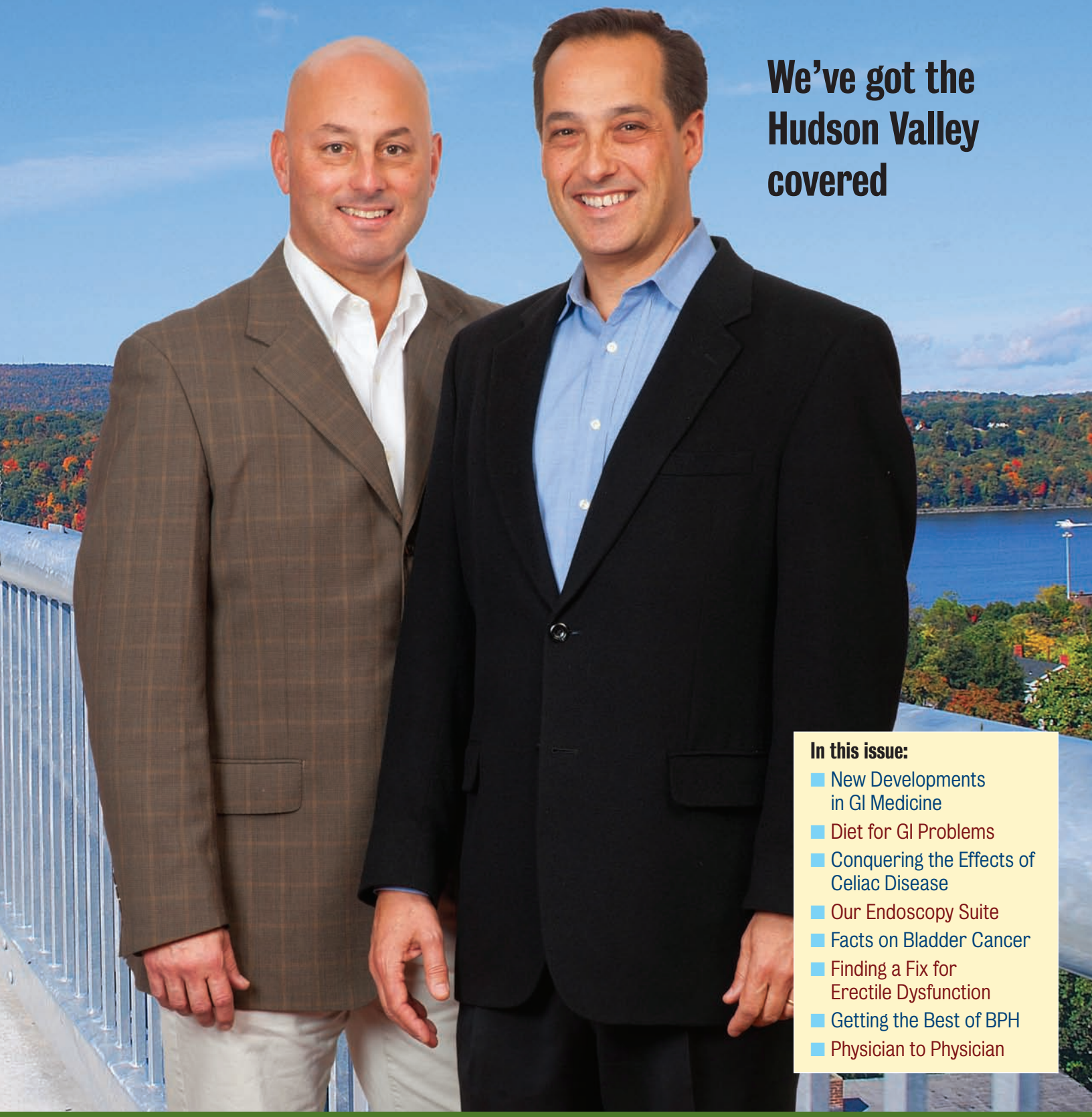
PremierHealth

The experience you need... the compassion you deserve

WINTER 2011



We've got the Hudson Valley covered

In this issue:

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

WE'VE GOT THE HUDSON VALLEY COVERED

Premier Medical Group

With offices in 3 Hudson Valley counties— which encompass Poughkeepsie, Fishkill, Kingston, Rhinebeck and New Windsor—and privileges at six area hospitals (St. Francis, St. Lukes, Northern Dutchess, Vassar Brothers Medical Center, Kingston Hospital, and Benedictine Hospital), the specialist physicians of Premier Medical Group are where our patients need us, right in their own neighborhoods.

MORE THAN 400 WALKERS TURNED OUT for Poughkeepsie's First Annual Great Prostate Cancer Challenge® Fun Walk on October 24, 2010. Sponsored by Premier Medical Group, the event raised over $50,000, most of which is to be divided between the Dyson Center for Cancer Care at Vassar Brothers Medical Center and the Eileen Hickey Center at St. Francis Hospital. The funds will be earmarked for prostate care such as free screenings and transportation.

Not only do we work in our patients' neighborhood, we are their neighbors, we live here too. The beauty of the Hudson Valley, the quality of life, and the valley's gracious citizens have helped Premier Medical attract physicians for whom the opportunity to practice top-notch medicine in first-rate surroundings is a combination they can't pass up.

As neighbors, we're committed to contributing to our community, not only maintaining what's good, but helping to make things better. That's why you'll hear our physicians offering advice on the radio, find them serving on community boards, hospital boards and committees, and meet them in your community centers and schools, where they provide educational programs like GI Teaching Day, and make sure as many valleyites as possible have access to and knowledge about preventive care.

Sometimes you'll find us walking along beside you, raising money for causes important to us all, doing the things a good neighbor should.

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

Gastroenterologists

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

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Khurram I. Ashraf, DO
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Srinivasan Selvaraj, MD
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Farshad Elmi, MD

Allied Professionals
Johanna Forlivio, RPA-C
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Urologists

With offices in Poughkeepsie, Kingston, Fishkill and Rhinebeck
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Daniel Katz, MD
Evan R. Goldfischer, MD, FACS
Michael Solliday, MD
Jason Krumholtz, MD
Scott Kahn, MD, FACS
Jose Sotolongo, MD
Naeem Rahman, MD
Paul Pietrow, MD, FACS
Michael Young, MD

Allied Professional
Kevin Torrens, RPA-C

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

PREMIER *medical group*

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[the future of medicine]

Staying on the Cutting Edge

Every day sees new developments in the science of medicine. The physicians of Premier Medical Group stay abreast of the news and make sure their patients benefit from the latest treatments.

Dr. Salvatore Buffa and Dr. Sunil Khurana attended this year's American College of Gastroenterology Annual Scientific Meeting and Postgraduate Course in San Antonio. Considered the premier GI clinical event of the year, this gathering offers educational programs presented by internationally-known experts and rising stars in the field of gastroenterology. Presentations address current clinical GI issues and also examine scientific developments on the horizon.

Upon their return to the Hudson Valley, Buffa and Khurana shared the information they had gleaned with their fellow GI Associates. Among the issues that made an impression…

Proton Pump Inhibitors for GERD and Ulcer Disease

Properly prescribed, the class of drugs known as proton pump inhibitors (PPIs)—which include such medicines as Nexium, Prilosec and Prevacid— are highly useful in reducing gastric acid for the treatment of GERD and ulcers of the stomach and small intestines.

• Recently, some questions have arisen about the safety of these drugs when taken by patients with cardiovascular disease who are also taking antiplatelet drugs like Plavix. New data presented from a major trial (called COGENT) showed no lowered survival in cardiac patients taking both drugs. In fact, PPIs substantially decreased GI bleeding in these patients.

• Contrary to some published reports, long-term PPI use does not increase the risk of osteoporosis. There is a statistical increase of hip fractures in patients on these medications, but the increase is small — rising from 3 fractures per 10,000 patients to 9 fractures per 10,000 patients.

New Hepatitis C Treatment on the Horizon

A new class of medicines, called protease inhibitors, are expected to be available for the treatment of Hepatitic C in the near future. When used in combination with the standard treatment of interferon and ribaviran, the new antiviral agents have the potential to nearly double the response rate compared to that of standard treatment alone. We will be following development of these drugs carefully in order to make them available to our patients as soon as appropriate.

Inflammatory Bowel Disease and Pregnancy

Biologic therapy has been proven successful in treating ulcerative colitis and Crohn's disease. Medications such as Remicade, Humira, or Cimzia — which block substances in the body that cause inflammation—have improved symptoms, healed mucosal damage and changed the natural course of the disease when initiated early.

• The newest research makes it clear that women with IBD who become pregnant must prepare to discontinue these medicines in the 3rd trimester of their pregnancies. At that time, such medications are transferred across the placenta and will affect the fetus.

Celiac Disease Flare-ups

Patients with gluten sensitive enteropathy (celiac disease) sometimes experience flare-ups of their symptoms even though they are carefully following a gluten-free diet.

• A number of potential causes for these episodes have been identified, including: unknowingly consuming products containing gluten, bacterial overgrowth, pancreatic insufficiency, microscopic colitis, irritable bowel syndrome and lymphoma.

MARCH IS COLON CANCER AWARENESS MONTH

• Colorectal cancer is the second leading cause of cancer deaths in the US. One in 18 Americans are at risk of getting colorectal cancer by the time they're 65.

• Don't be a statistic... when found in its early stages, colorectal cancer is highly treatable.

Initial colonoscopy screening should begin at age 50 in otherwise healthy individuals. Nearly 40% of people over age 50 have never been adequately screened for this disease.

Remember, early detection is your best defense!

FREE HEALTH SCREENINGS

Premier Medical Group of the Hudson Valley works in partnership with the Cancer Services Program, a state and federally-funded program which offers free breast, cervical and colorectal screenings and follow-up services for uninsured men (50–64) and uninsured women (40-64) living in Ulster and Dutchess counties.

For more information, call 1-866-442-2262.

EASING YOUR GI CONDITION WITH Dietary Measures

You're GI physician will usually counsel about the kind of diet that's best for what ails you, but it's only the individual who can apply the diligence and willpower to follow that advice.

Looking Out for Hidden Lactose

Lactose intolerance is the inability to digest lactose, a sugar found in milk and milk products. The condition is caused by a deficiency of the enzyme lactase, which is produced by the cells lining the small intestine. That enzyme breaks lactose down into two simpler forms of sugar—glucose and galactose,—which are then absorbed into the bloodstream.

People with lactose intolerance may feel uncomfortable 30 minutes to 2 hours after consuming milk and milk products. Symptoms range from mild to severe, based on the amount of lactose consumed and the amount an individual is able to tolerate.

It's relatively easy to avoid milk and milk products such as butter, cheese, or ice cream. But, since small amounts of lactose are frequently added to processed foods, people with a very low tolerance for lactose need to stay vigilant. They'll need to read food labels carefully and stay alert to words like "whey" or "curds" as well as "milk".

Scrutinize the labels on:

- Bread, biscuits, cookies and other baked goods
- Processed breakfast foods, including cereals, toaster pastries, frozen waffles and pancakes
- Instant products, such as potatoes, soups, and mixable beverages
- Potato or corn chips, and other snacks
- Luncheon meats—unless they're kosher—as well as bacon, sausage, and hot dogs
- Liquid and powdered meal replacements
- Non-dairy creamers and whipped toppings
- Margarine
- Salad dressings
- About 20 percent of prescription medicines contain lactose, so people with severe lactose intolerance should check with their pharmacist before starting on a new drug.

MONKEY BUSINESS IMAGES/DREAMTIMES.COM

Eating Right For Irritable Bowel Syndrome

Irritable bowel syndrome (IBS), one of the most common disorders affecting Americans, is commonly characterized by a set of symptoms that includes cramping, abdominal pain, bloating, constipation, and diarrhea. Most people with IBS can control these symptoms with a combination of diet, stress management, fiber supplementation and, occasionally, prescription drugs.

Because of the variety of symptoms that need to be addressed, and individuals' varying responses to foods, there's no single diet for IBS. But there are some foods and dietary practices that are generally associated with worsening or improving symptoms.

Before making dietary changes, it's a good idea to keep a food journal noting the foods that seem to cause you distress. Discuss the findings with your physician and, together, you'll be able to come up with a dietary approach that improves your condition.

Make a point of talking to your doctor about fiber. In many cases, dietary fiber may lessen IBS symptoms, particularly constipation. However, it may not help with lowering pain or decreasing diarrhea. High-fiber diets keep the colon mildly distended, which may help prevent spasms, but this approach doesn't suit every patient.

Foods and beverages that may make IBS worse include:

- fatty foods, like french fries
- milk products, like cheese or ice cream (about 40% of people with IBS are lactose intolerant)
- chocolate
- alcohol
- caffeinated drinks, like coffee and some sodas
- Gas-producing foods, such as beans, onions, broccoli, and cabbage may aggravate symptoms.
- Carbonated drinks can introduce gas into the intestines, causing abdominal pain.
- Large amounts of the sugar substitutes mannitol or sorbitol can cause excess gas, bloating, cramping and diarrhea.
- Large meals can cause cramping and diarrhea, so try eating smaller meals more often.
- Try to slow down how fast you eat.

CONQUERING THE EFFECTS OF Celiac Disease

A careful diet does the trick, and gluten-free can mean symptom-free for millions of Americans afflicted with this genetic disease of the small intestine.

It's not a food allergy or a sensitivity to certain grains. Celiac disease (CD) is a chronic inflammatory or immune disease of the small intestine that interferes with absorption of nutrients from food. People with CD can't tolerate gluten, a protein found in wheat, rye and barley. When they do consume gluten, their immune systems respond by damaging or destroying the villi—tiny, fingerlike protrusions lining the small intestine—which normally allow nutrients to be absorbed through the walls of the small intestine into the bloodstream. Without healthy villi, a person becomes malnourished, no matter how much food he or she consumes.

Celiac disease was once thought to be a rare childhood syndrome, but is now recognized as a common genetic disorder that can first appear at any age. About 5–10 percent of people who have a first-degree relative diagnosed with CD —a parent, sibling, or child—are likely to have it as well. In the U.S., it's estimated that close to 3 million people have CD, but the majority haven't been diagnosed.

The problem is that, even for people who don't experience symptoms, long-term celiac disease can cause complications, including malnutrition—leading to anemia, osteoporosis, and miscarriage, etc.—liver diseases, and cancers of the intestine.

Testing can tell

Recognizing celiac disease can be difficult because some of its symptoms are similar to those of other diseases. CD can be confused with irritable bowel syndrome, iron-deficiency anemia caused by menstrual blood loss, inflammatory bowel disease, diverticulitis, intestinal infections, and chronic fatigue syndrome. The National Institutes of Health has launched a Celiac Disease Awareness Campaign and, as doctors are alerted to the many varied symptoms of the disease, diagnosis rates are increasing.

Before testing, you should continue to eat foods containing gluten, such as breads and pastas. If you stop consuming gluten in advance, the results may be negative for celiac disease even if the disease is present.

Foods, medicines, cosmetics, and other products made with wheat, rye or barley contain the gluten that is harmful to people with celiac disease.

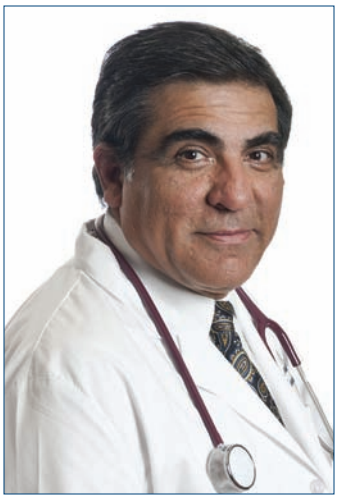
Recently developed blood tests are making the process easier. People with celiac disease have higher than normal levels of certain auto-antibodies— proteins that react against the body's own cells or tissues—in their blood. If blood tests and symptoms suggest CD, endoscopy is used to perform a biopsy of the small intestine and confirm the diagnosis by checking for damage to the villi.

Doing it with diet

Currently, the only treatment for celiac disease is a gluten-free diet. For most people, this diet will stop symptoms, heal existing intestinal damage, and prevent further damage. Improvement begins within days of going gluten-free.

To stay well, people with celiac disease must avoid gluten for the rest of their lives, as even a small amount can damage the small intestine.

Luckily, CD sufferers aren't on their own: these days, supermarket shelves bulge with gluten-free products, restaurants rise to the challenge of providing tasty alternatives, and your physician can help you eat your way to good health.



Sunil K. Khurana, MD

"We GI physicians are well aware of the incidence of celiac disease. But most patients start looking for help with their primary physicians. Unfortunately, the symptoms of this disease can be so vague that primaries just don't think of it in cases where the typical digestive problems aren't present.

The new thinking is, before we diagnose anyone as having irritable bowel syndrome, we need to rule out celiac. If people are anemic, vitamin deficient, or have metabolic disorders, the physician has to rule out celiac. As a result, our threshold for ordering tests for celiac disease is very low. And we tell our patients that if their mom, dad, or a sibling has celiac, they should be tested for it, since the disease is genetic—that is, it runs in families.

In celiac disease, treatment is basically diet. After all, why use a drug if diet can solve the problem? The way our patients respond to the diet really depends on the individual. I've observed that people with severe symptoms feel so wonderful once they're on the diet, they stick to it. Sometimes you don't realize how bad you're feeling until you feel good."

PREMIER MEDICAL'S

Endoscopy Suite

Premier Medical's Endoscopy Suite is home base for the specialist physicians of GI Associates and Hudson Valley Urology, divisions of Premier Medical Group.

Pictured above are Dr. Sven Hida of GI Associates (left) and Dr. Jason Krumholtz of HVU with members of the Endoscopy Suite staff (from left to right) Judy Martinez, Lisa Gray, and Adele Lawler.

For years, the Endoscopy Suite at 243 North Road in Poughkeepsie has been the active center for procedures performed by the physicians of GI Associates. In 2011, with the addition of a new, state-of-the-art headquarters designed specifically for urological procedures, the physicians of Hudson Valley Urology have joined them. Now, both divisions of Premier Medical Group call this high-tech, patient-centered facility home.

To efficiently undertake the more than 4000 endoscopy procedures GI Associates performs here every year requires a well-designed team approach. Beginning with the physical layout of the suite, the choice of medical equipment, and the creation of a congenial environment, every aspect of the Suite is devoted to achieving successful outcomes and patient comfort.

"There's everything a physician could need in this center," says Dr. Salvatore Buffa, "and everything necessary to put our patients at ease. We have a dedicated, board-certified

en·dosco·py — visual examination of the interior of a hollow body organ or cavity by use of an an illuminated, flexible fiberoptic camera (endoscope).

anesthesiologist who knows how we work. The experienced nurses assisting in GI procedures have all been specialized GI nurses for over 20 years. They're highly trained and knowledgeable about the procedures. And when patients are in the recovery room, they're being looked after by nurses who are alert to potential problems, side effects and post-procedure discomfort."

"The majority of GI Associates' endoscopic procedures are done in the suite," Dr. Buffa says. "However, for those patients who have serious comorbid conditions, we may opt to have the procedures done within a hospital setting to obviate risk on the mere chance that something might occur."

HVU comes to North Road

The details involved in creating a suite dedicated solely to urological procedures—selecting new state-of-the-art medical equipment, designing the physical layout, and establishing the treatment protocols—take a great deal of planning. And ultimately, all that planning is devoted to maximizing patient privacy and comfort, as well as devising an environment conducive to the optimum in medical care.

"Everything we've learned in 12 years of practicing these procedures was brought to bear in the design of this suite," says HVU's Dr. Evan Goldfischer. "And while we were creating it, we knew we had to live up to the name Premier."

"Since the site has been designed purely for procedures, it doesn't have to accommodate all the other interactions that go on in a doctor's office," says Patty Sullivan, Director of Clinical operations for HVU. Sullivan previously managed the operating room at St. Francis Hospital and brought her considerable knowledge and experience to bear on the new urology center.

"It's not just about efficiency," Sullivan says, "but also about safety in all three areas… the pre-op, inter-op, and post-op rooms. We totally reimagined and reengineered the pre-existing space, changing the room design and dimensions to accommodate patient needs.

"We've paid careful attention to such things as traffic flow. For instance, patients won't have to walk down a hallway to get from one setting to another. And we've done everything possible to maintain the patients' privacy while allowing for them to be carefully monitored by doctors and nurses.

"We feel we've done a premier job in integrating safety and privacy concerns. We've been able to create a place where patients are made comfortable and treated with respect," says Sullivan.

Dr. Goldfischer is especially pleased with the new equipment the practice has selected for urological procedures, some of which is new to the region.

"The new equipment manufactured by Karl Storz, a leading medical instrument company, includes state-of-the-art digital cameras with high-definition flat screen monitors," says Dr. Goldfischer. "They give us gorgeous, detailed views that reveal subtle tissue states. The streamlined design of the cystoscopes really aids patient comfort. Also, the ergonomic design of these instruments, which are comfortable to handle, allow us to better focus on the task at hand, with less fatigue and enhanced precision."

"This practice seems to constantly focus on doing it better," says Sullivan. "We are continuously reassessing and reevaluating our processes and instrumentation, looking for the next best thing. HVU doesn't rest on its laurels."

cystoscopy (sis-tos-scope-y)— endoscopy of the urinary bladder via the urethra, using a cystoscope.

Salvatore M. Buffa, M.D.

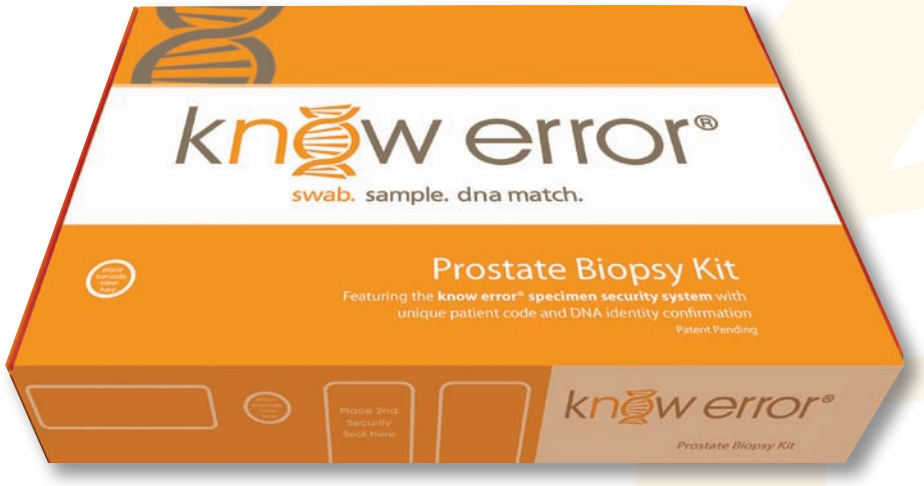
"This is the central hub for our endoscopy procedures. In this facility we've gathered a highly-trained staff, a team that's familiar with the individual rhythms and approaches of the endoscopy physicians. On the GI side, more than 4,000 procedures are performed in the Suite annually.

We have a dedicated, board-certified anesthesiologist who is familiar with our operation. And we've invested in state-of-the-art equipment that includes high-definition monitors to aid in viewing any condition where subtle findings can be significant.

The actual endoscopy procedures take about the same time to perform in our Suite as they would in a hospital setting. But here our patients will find the preop and postop times far more expedient, and we've worked hard to create a congenial environment.

GI patients can benefit from the comfort of familiar surroundings, as the Suite is right across the hall from the offices where they originally came to see their GI for a consult. When a patient wakes up in post-op and has questions, we're right there at their bedside to answer them."

A Partnership in Patient Safety



In an effort to provide the most accurate diagnosis possible, Hudson Valley Urology utilizes the **know error® system** for prostate biopsies. This system uses bar coding and DNA matching to ensure that, when your results arrive, the results belong to you.

Together we deliver an important measure of safety for prostate biopsy patients.

know error®

swab. sample. dna match.

For more information | **www.knowerror.com**

GREAT PROSTATE CANCER Challenge® 2010

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WHAT YOU NEED TO KNOW ABOUT

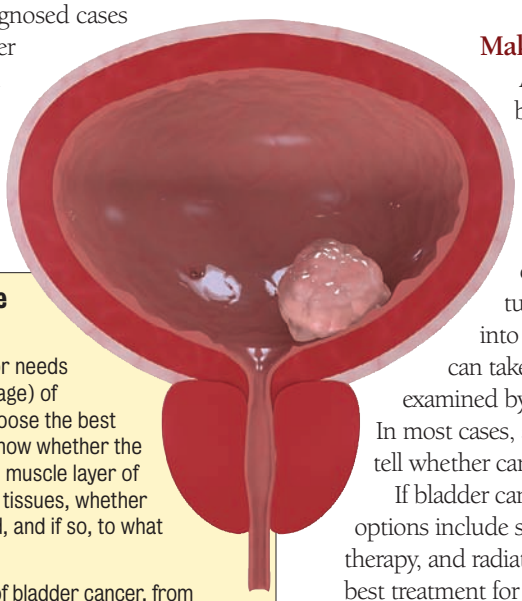
Bladder Cancer

It's the sixth most common cancer diagnosed in the U.S. (the fourth most common for men), and while the number of cases has been rising, cure-rates are very good when the disease is diagnosed early.

The most important thing to know about bladder cancer is that smoking tobacco is the greatest risk factor for developing the disease. Smokers are twice as likely to get bladder cancer as non-smokers. Long-time smokers are at greater risk than short-timers who have quit: studies show that in the first four years after a smoker quits, his risk of developing bladder cancer decreases by 40 percent.

People who come in contact with toxic chemicals in the workplace are at higher risk too. This includes workers in the dye, rubber, chemical, metal, textile, and leather industries, as well as hairdressers, machinists, printers, painters, and truck drivers. If they're also smokers, the risk is compounded and their need for vigilance increased.

Bladder cancer is now the sixth most common cancer in the US. There has been a steady climb in the number of diagnosed cases (70,000 in 2010) over the last 20 years, but early detection and treatment advances have actually brought the death rate down.



Staging the disease

If bladder cancer is diagnosed, your doctor needs to learn the extent (stage) of the disease to help choose the best treatment. Tests will show whether the tumor has invaded the muscle layer of the bladder or nearby tissues, whether the cancer has spread, and if so, to what parts of the body.

There are five stages of bladder cancer, from Stage 0 to Stage 4. In Stage 0, as shown in the illustration, cancer cells are found only on the surface of the inner lining of the bladder. In almost 3 out of 4 cases, patients are first diagnosed with bladder cancer when their cancer is confined to the bladder.

The first indication of bladder cancer is usually the appearance of blood in the urine (hematuria). There may be enough blood to notice a reddish cast to the fluid or it may occur in microscopic quantities visible only through a laboratory test. Other possible symptoms include:

- Feeling an urgent need to empty your bladder
- Having to empty your bladder more often than you used to
- Feeling the need to empty your bladder without results
- Needing to strain (bear down) when you empty your bladder
- Feeling pain when you empty your bladder

Of course, these symptoms—as well as hematuria—could be caused by other health problems, but it's crucial that they not be ignored. Be it bladder cancer or some other condition, early diagnosis can be key to successful treatment.

Making the diagnosis

At Hudson Valley Urology we begin the diagnosis process by having our lab check the patient's urine for blood, cancer cells, and other signs of disease. The physician will perform a cystoscopy, using a thin, lighted tube (a cystoscope) to look directly into the bladder. At the same time he can take tissue samples (biopsy) to be examined by our pathologist for cancer cells. In most cases, a biopsy is the only sure way to tell whether cancer is present.

If bladder cancer is detected, treatment options include surgery, chemotherapy, biological therapy, and radiation therapy. To decide on the best treatment for a patient, the physician takes into account the grade of the tumor (which tells how fast it's likely to grow or spread), the stage of the cancer, and the patient's general health.

The specialists at HVU are committed to caring for their bladder cancer patients every step of the way.

Michael Solliday, M.D.

"We usually see patients with bladder cancer after microscopic blood is found in their urine during standard checkups. Often, there are no other apparent symptoms. From diagnosis, to treatment, to surveillance—at HVU we're able to care for patients with bladder cancer at any stage of the disease.

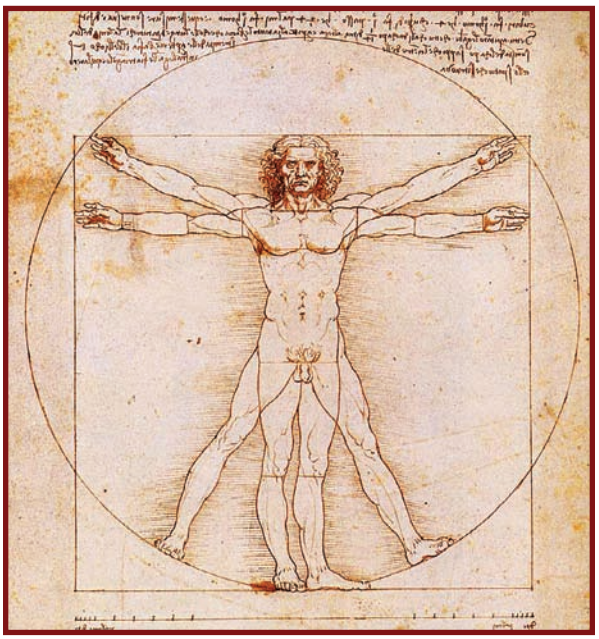
HVU has been involved in multiple clinical trials of drugs and procedures to prevent progression and recurrence of the disease. Some of the approaches we've tested are now becoming the standard of treatment for bladder cancer.

Even when bladder cancer is diagnosed early and successfully treated, there's a real risk of recurrence. That's why surveillance is so important, and we strictly adhere to the medical guidelines for long-term follow-up testing and examination.

The likelihood of recurrence actually doubles if a patient keeps on smoking, so we work with smoking cessation groups to try to eliminate this risk factor. Lifestyle plays a big role. If people stopped smoking, had healthier diets, and exercised more, we'd see a lot fewer cancers."

FINDING A FIX FOR Erectile Dysfunction

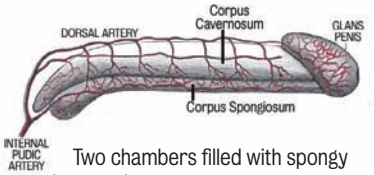
Now that scientists know the causes, and have devised a number of treatments to deal with them, this age-old condition is something worth talking about, and that's good news for the 30 million American men who have ED.



Simply put, erectile dysfunction (ED) is the inability of a man to get or maintain an erection firm enough for satisfactory sexual intercourse. It is, of course, a condition that's been with us through the ages and, until relatively recently, the sort of problem that men (and their partners) suffered in silence. For centuries it was believed that ED was the result of supernatural activity, the anger of the gods or a witch's curse. In later times, the cause was thought to be purely psychological or linked to some moral failing.

In the 21st century, the age of embarrassed silence about ED has ended. With scientists having achieved greater understanding of the physiological mechanisms involved in men's sexual health, and with a number of treatment options now available, talking about ED has become the first step in resolving the condition.

As with most bodily functions, achieving an erection requires a precise sequence of events, and ED can occur when any of the necessary events is disrupted. At least 75% of ED is the result of a physical cause, such as disease, injury, or the side effects of drugs. While the condition is most common in older men, ED is not an inevitable part of aging. In fact, it is treatable at any age.



Two chambers filled with spongy tissue—the corpora cavernosa—run the length of the penis. The spongy tissue contains smooth muscles, fibrous tissues, spaces, veins, and arteries. A membrane—the tunica albuginea, surrounds the corpora cavernosa. The urethra, which is the channel for urine and ejaculate, runs along the underside of the corpora cavernosa and is surrounded by the corpus spongiosum.

The mechanics of male sexual response

- An erection begins with sensory or mental stimulation, or a combination of both.
- Impulses in the brain, spinal column, and area around the penis cause the muscles of the corpora cavernosa to relax, allowing blood to flow in through the arteries and fill the spaces.
- The blood creates pressure in the corpora cavernosa, making the penis expand.
- The tunica albuginea helps trap the blood in the corpora cavernosa, which sustains the erection.
- The erection ends when muscles in the penis contract to stop the inflow of blood and open the veins for blood outflow.

Any disorder that causes injury to the involved nerves or impairs blood flow in the penis has the potential to cause ED. Diseases— such as diabetes, high blood pressure, nerve disease or nerve damage, multiple sclerosis, atherosclerosis, and heart disease—account for the majority of ED cases. The lifestyle choices that contribute to heart disease and vascular problems also raise the risk of ED. Smoking, excessive alcohol consumption, being overweight, and not exercising may also be causes of ED.

Many common medicines—such as blood pressure drugs, antihistamines, antidepressants, tranquilizers, appetite suppressants, and cimetidine, an ulcer drug—may disrupt the mechanics of erection and lead to ED. It's estimated that less than 25% of ED is primarily caused by psychological factors such as stress, anxiety, guilt, depression, low self-esteem, and fear of sexual failure. Yet, even when ED has a mainly physical cause, it's possible for psychological factors to make the condition worse.

Fixing the machinery

Treatment begins with the taking of a medical/sexual history. This is important for defining the

degree and nature of the ED and gaining insight into the diseases or medications that may be causing it. A physical exam and sometimes simple laboratory tests may reveal systemic problems behind ED. A blood test to measure the amount of available testosterone in the blood, for example, may yield information about an endocrine problem (low testosterone) that could explain why a patient has decreased sexual desire.

Some men may be able to regain sexual function by making healthy lifestyle changes such as quitting smoking, reducing alcohol consumption, losing weight, and increasing physical activity. Others may be counseled on cutting back or replacing medicines that could be causing ED. Most will find help in one of the medicines that have become the mainstay of ED treatment.

Sildenafil (Viagra®)—the first oral medication to treat ED—was approved for use by the FDA in 1998. Hudson Valley Urology, a division of Premier Medical Group, took part in the clinical trials gauging its safety and effectiveness, as well in the clinical trials for vardenafil HCI (Levitra®) and tadalafil (Cialis®), which were approved in 2003.

These three medications belong to a class of drugs called phosphodiesterase-5 (PDE-5) inhibitors. They all work by enhancing the effects of nitric oxide, a chemical created in the body that relaxes smooth muscles in the penis in response to sexual stimulation and allows the increased blood flow needed for erection. The drugs are equally effective — helping about 70 percent of men who take them —but differ in the standard dose, length of the effect, how they interact with food and other medications, and the side effects that can accompany them.

Managing the motivation

Successful as the PDE-5 inhibitors may be in solving physical problems, a history of ED can leave a patient anxious about performance. It's not uncommon to need to try ED medication a few times before feeling comfortable enough to fully respond. And it's important to remember that the medications will not result in erection without the presence of sexual stimulation. They are not designed to treat a lack of sexual desire, a different situation than experiencing desire but being unable to maintain an erection.

In such situations, a low testosterone level (low-T) could be the culprit. The National Institute of Health estimates that about 5 million American men have low T. In medical studies, about 70 percent of men with low-T reported experiencing ED, and more than 60 percent reported a low sex drive. As Dr. Goldfischer observes, "if you're brain isn't bathed in testosterone, you won't experience satisfactory erections."

Testosterone, produced mainly in the testes, is the most important male sex hormone. Testosterone levels naturally decrease with age. Disease, accidents and certain drugs also affect production of the hormone. Men with type 2 diabetes are twice as likely as the rest of the male population to have low testosterone.

Since the symptoms of low testosterone are similar to many other conditions — including ED, depression, and lack of energy—it often goes undiagnosed. Yet a simple blood test gives definitive results and there are several treatment options available—such as gels, patches or injections—that increase the amount of testosterone in your body.

Your physician will help you decide if you're a good candidate for testosterone replacement and, if so, advise on the pros and cons of the different treatments.

For the minority of men for whom oral medication isn't sufficiently helpful, and for those who prefer a non-pharmacological solution, there are several additional treatment options that Hudson Valley Urology can provide.

Many men will be able to achieve stronger and more immediate erections by injecting drugs into the penis, causing it to become engorged with blood. Mechanical vacuum devices cause an erection by creating a partial vacuum, which draws blood into the corpora cavernosa. An elastic ring around the base of the penis maintains the erection during intercourse by preventing blood from flowing back into the body.

Significant advancement in the development of prosthetic devices that can be surgically implanted now provides several different options. Each of these approaches require some getting used to and have varying degrees of side effects. Usually, the men who opt for them are pleased with the results.

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.

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

Evan R. Goldfischer, MD

"There are two ways to look at ED, from the psychological angle and as a matter of mechanics. Most importantly, you have to get the blood to the penis to experience an erection. But even if you have lots of blood flow, if your brain isn't sufficiently bathed in testosterone, you won't experience satisfactory erections.

For blood flow, the PDE-5 inhibitors are the mainstay of treatment. But some of the drugs have requirements or side-effects that individual patients can't accommodate, so it's important to have several to choose from. We run many clinical trials to help develop new options for our patients.

Testing and treatment for low testosterone are both very easy. We have injections, gels, patches, little pellets that go under the skin. We help our patients work out the pros and cons of each method.

What we like to do more of is to counsel men to get healthier. All of those things that make you healthier — diet, exercise, smoking cessation—will help your ED. I like to say that the penis is a barometer for cardiovascular health. Sometimes the first symptom of cardiovascular disease is ED. There's more and more data suggesting that men who develop ED should consult a physician about their heart."

[urology]

GETTING THE BEST OF BPH

Benign Prostatic Hyperplasia is the medical name for enlargement of the prostate. It's a common condition, affecting more than 50 percent of men in their sixties. Whether your symptoms are mild or severe, we can make them better.

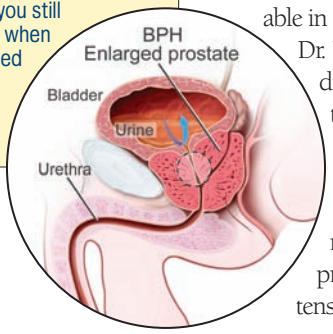
As common a part of aging as getting gray hair, prostate enlargement is a condition that the majority of men will have to deal with at some point in their lives. By the time they're in their seventies, as many as 90 percent of men experience some symptoms of BPH.

As the prostate enlarges, the gland begins to press against the urethra—the tube that transports urine out of the body—like a clamp on a garden hose. As a result of the pressure, the bladder wall becomes thicker and irritable and, eventually, the bladder begins to contract even when it contains only small amounts of urine, causing more frequent urination. In time, the bladder weakens and loses the ability to fully empty itself.

Sound Familiar?

If you have BPH, you may have one or more of these problems:

- A frequent and urgent need to urinate. You may get up several times a night to go to the bathroom.
- Trouble starting a urine stream. Even though you feel you have to rush to get to the bathroom, you find it hard to start urinating.
- A weak stream of urine
- A small amount of urine each time you go
- The feeling that you still have to go, even when you've just finished urinating
- Leaking or dribbling urine



The BPH Problem

It's this narrowing of the urethra and partial emptying of the bladder that cause many of the problems associated with BPH. Symptoms and their severity vary. In fact, you may not even know you have an enlarged prostate until your physician discovers it during a routine checkup. But, if you experience urinary problems such as those described in the box above, it's important to consult your physician. Though about 80 percent of such symptoms will result in a diagnosis of BPH, they can also signal other, more serious conditions that require prompt treatment. These conditions, including prostate cancer, can be ruled out only by a doctor's examination.

By itself, BPH is usually not a serious condition, unless the symptoms are so troublesome that you can't enjoy life. However, over time, severe BPH could cause problems. Urine retention and strain on the bladder can lead to urinary tract infections, bladder or kidney damage, bladder stones, and incontinence—the inability to control urination. If the bladder is permanently damaged, treatment for BPH may be ineffective.

The BPH Solutions

"Medicines for BPH are available in two categories," says Dr. Kahn. "One type of drug shrinks the prostate and the other, alpha-blockers, work by reducing the tension in the smooth muscle of the prostate. If we use a tension reducer, patients can see results within a week, while prostate size-reducing drugs typically take 3 to 6 months for results," he says.

For some men, minimally-invasive surgery will provide the best results over the long term, but the side effects are greater than with medication. At Hudson Valley Urology, we perform a wide range of procedures, enabling us to offer the approach that's best suited to a patient's health status and symptoms.

The ideal candidate for TUNA (transurethral needle ablation) for example, says Dr. Kahn, is someone with a moderately enlarged prostate and moderate post-void residuals who hasn't responded to drug treatment. A patient with a greatly-enlarged prostate, severe symptoms, and large post-void residual might better benefit from a laser prostatectomy. We review the pros and cons of each approach with our patients and, together, choose the one that's right for them.

Scott Kahn, MD FACS

"When men are referred to us with urinary problems, the first thing on their minds is a concern about prostate cancer. A careful workup addresses that concern, but more often results in a diagnosis of BPH.

Treatment options range from watchful waiting, to medicines, to minimally invasive procedures like TUNA or laser prostatectomy, which can be done right here in the office. The choice of treatment generally depends on how severe the symptoms are.

Part of the evaluation we do is an AUA symptom score — it's an important tool for categorizing symptoms as mild, moderate or severe. If the AUA score is low and PSA levels are low, we might recommend watchful waiting in the hope the symptoms will clear up on their own. For moderate to severe symptoms, we'll consider intervention.

I'd say a good 95 percent of our patients are satisfied with their treatment results, whether it's medicinal or surgical treatment that's initiated. We offer the full array of approaches. If one approach doesn't work, there is almost always another option to try. We constantly have clinical trials underway that allow us to continue helping the patient until he gets the results he needs."

PremierHealth 12

*IN THE TREATMENT OF SYMPTOMATIC BPH**

RAPID RELIEF

THAT KEEPS HIM GOING

*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

Watson

RAPAFLO® 8 mg (silodosin) capsules

READY. SET. GO.

06318 1/10

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

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800-272-5525
For additional information see:
www.rapaflo.com
or call 1-866-RAPAFLO (727-2356)

Rx Only Revised: November 2009 173761-2 S1109

Physician to Physician

Insight regarding Premier Medical Group's capabilities and concerns

Introductions

Three physicians bring new talents to the GI Associates team

We are very pleased to welcome three new additions to our physician staff," says Dr. Sunil Khurana, senior physician at GI Associates, a division of Premier Medical Group. "Each brings us a unique set of capabilities, insights and commitment."

"Dr. Elmi trained at Yale, where he took advanced fellowship training in endoscopic ultrasound (EUS) and ERCP. With an additional degree in Clinical Investigation, he brings a wealth of knowledge. Dr. Hida has extensive computer experience and we expect he will be invaluable in helping to lead us into the new era of electronic medical records and methodical approaches to quality issues. Dr. Selveraj brings us twenty years of practice experience and a fine academic background wherein he taught a generation of medical residents and gastroenterology fellows at Our Lady of Mercy Medical Center, a major teaching center affiliated with New York Medical College."

Farshad Elmi, MD, MSc

"I joined GI Associates because of the intellectual curiosity of the physicians practicing in the group. GIA offers a high level of care to patients in the community and I believe my focus on gastrointestinal oncology and diagnostic and interventional EUS will be a good fit. I have received academic training on designing and conducting patient-oriented research and have published many abstracts, manuscripts and book chapters. The practice's commitment to research will give me the opportunity to maintain my scholarly activities."

Sven Hida, MD

"My wife is from Poughkeepsie, so I know the area well and it appeals to me in many ways. At GI Associates, I really like the camaraderie and the way patients are treated. I like that we have weekly meetings to discuss articles and papers, something you don't often find in the private sector. I speak five languages, including Spanish in which I'm fluent. Since some of my patients speak only Spanish, that's comforting for them."

Srinivasan Selvaraj, MD

"This is a progressive group that's doing a lot of clinical trials and investigational work. They're very interested in education, attending conferences, and performing hard science, and this truly suits my approach to medicine. Aside from having more than 20 years of clinical and teaching experience, my special area of interest is capsule endoscopy and GI Associates will give me the opportunity to bring all these skills to bear."

Clinical Trials CONNECTION

We are currently seeking patients to participate in studies in:

BPH/Nocturia
Alexa Markiewicz • 845-437-5051
amarkiewicz@premiermedicalhv.com

Crohn's Disease
Alyson Cahill • 845-451-7262
acahill@premiermedicalhv.com

Erectile Dysfunction
Kimberly LaVigne-Secord • 845-437-5002
ksecord@premiermedicalhv.com

Female Sexual Dysfunction
Ann Scandariato • 845-437-5010
ascandariato@premiermedicalhv.com

Gout
Jeanie Loeffel • 845-437-3810
jloeffel@premiermedicalhv.com

Interstitial Cystitis
Kimberly LaVigne-Secord • 845-437-5002
ksecord@premiermedicalhv.com

Irritable Bowel Syndrome
Alyson Cahill • 845-451-7262
acahill@premiermedicalhv.com

Kidney Stones
Jeanie Loeffel • 845-437-3810
jloeffel@premiermedicalhv.com

Overactive Bladder
Alexa Markiewicz • 845-437-5051
amarkiewicz@premiermedicalhv.com

Premature Ejaculation
Kimberly LaVigne-Secord • 845-437-5002
ksecord@premiermedicalhv.com

Prostate Cancer
Ann Scandariato • 845-437-5010
ascandariato@premiermedicalhv.com

Ulcerative Colitis
Alyson Cahill • 845-451-7262
acahill@premiermedicalhv.com

- 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]

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

HUMIRA®
adalimumab

IMPORTANT SAFETY INFORMATION[1]

WARNINGS
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 infection 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.**

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.

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.

Serious Infections
Do not start HUMIRA in patients with an active infection, including localized infections. 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, or patients who have resided or traveled in regions where TB or mycoses, such as histoplasmosis, coccidioidomycosis, or blastomycosis, are endemic. Treatment of latent TB infection prior to therapy with TNF-blocking agents has been shown to reduce the risk of TB reactivation during therapy. When TB skin testing is performed, an induration size of 5 mm or greater should be considered positive, even if vaccinated previously with Bacille Calmette-Guerin (BCG). HUMIRA should be discontinued if a patient develops a serious infection or sepsis. Patients who develop a new infection should undergo a prompt and complete diagnostic workup, and appropriate antimicrobial therapy should be initiated.

Malignancies
More cases of malignancies were observed among patients receiving TNF blockers, including HUMIRA, compared to control patients in clinical trials. These malignancies, other than lymphoma and non-melanoma skin cancer, were similar in type and number to what would be expected in the general population. In the controlled and open-label portions of HUMIRA clinical trials, there was an approximately 3-fold higher rate of lymphoma than expected in the general population. Postmarketing cases of acute and chronic leukemia were reported with TNF blocker use.

Postmarketing cases of malignancies, some fatal, were reported among children, adolescents, and young adults receiving TNF blockers, of which HUMIRA is a member. Approximately half of these were lymphomas; other cases included rare malignancies associated with immunosuppression and malignancies not usually observed in children and adolescents. The malignancies occurred after a median of 30 months of therapy (range 1 to 84 months). Most patients were receiving concomitant immunosuppressants.

The potential role of TNF-blocking therapy in the development of malignancies is not known.

Hypersensitivity
Anaphylaxis and angioneurotic edema have been reported rarely following HUMIRA administration.

Hepatitis B 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. For patients identified as carriers of HBV, exercise caution when prescribing HUMIRA, with careful evaluation and monitoring prior to and during treatment. HUMIRA should be stopped and antiviral therapy should be initiated in patients who develop hepatitis B reactivation.

Neurologic Reactions
TNF-blocking agents, including HUMIRA, have been associated with rare cases of new onset or exacerbation of central nervous system demyelinating disease, including multiple sclerosis, and peripheral demyelinating disease, including Guillain-Barré syndrome. Exercise caution when considering HUMIRA for patients with preexisting or recent-onset central or peripheral nervous system demyelinating disorders.

Hematologic Reactions
Rare reports of pancytopenia including aplastic anemia have been reported with TNF-blocking agents. Medically significant cytopenia (e.g. thrombocytopenia, leukopenia) has been infrequently reported with HUMIRA. The causal relationship of these reports to HUMIRA remains unclear.

Congestive Heart Failure
Worsening congestive heart failure (CHF) has been observed with TNF-blocking agents, including HUMIRA, and new-onset CHF has been reported with TNF-blocking agents.

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.

Drug Interactions
Serious infections were seen in studies with concurrent use of anakinra and another TNF-blocking agent; therefore, the combination of HUMIRA and anakinra is not recommended.

Adverse Reactions
In the placebo-controlled clinical studies of adult patients with rheumatoid arthritis, the most frequent adverse reactions vs placebo were injection site reactions (20% vs 14%), upper respiratory infection (17% vs 13%), injection site pain (12% vs 12%), headache (12% vs 8%), rash (12% vs 6%), and sinusitis (11% vs 9%). Discontinuations due to adverse events were 7% for HUMIRA vs 4% for placebo.

In HUMIRA clinical trials for ankylosing spondylitis, psoriatic arthritis, Crohn's disease, and plaque psoriasis, the safety profile for patients treated with HUMIRA was similar to the safety profile seen in patients with rheumatoid arthritis. In the placebo-controlled clinical trials in plaque psoriasis, the incidence of arthralgia was 3% in HUMIRA-treated patients versus 1% in controls.

In general, the adverse reactions in juvenile idiopathic arthritis (JIA) patients were similar in frequency and type to those seen in adult patients. Severe adverse reactions reported in the clinical trial in JIA included neutropenia, streptococcal pharyngitis, increased aminotransferases, herpes zoster, myositis, metrorrhagia, and 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. The safety of HUMIRA in pediatric patients for uses other than JIA has not been established.

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

Please see brief summary of full Prescribing Information on last pages of this advertisement.

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WARNINGS

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, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis before HUMIRA use and during therapy. Treatment for latent infection 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.**

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 tuberculosis in patients who tested negative for latent tuberculosis 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.

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 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 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 of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis. HUMIRA can be used alone or in combination with DMARDs.

Ankylosing Spondylitis HUMIRA is indicated for reducing signs and symptoms in 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

Serious Infections (see also Boxed Warning) Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients receiving TNF-blocking agents. Among opportunistic infections, tuberculosis, histoplasmosis, aspergillosis, candidiasis, coccidioidomycosis, listeriosis, and pneumocystosis were the most commonly reported. Patients have frequently presented with disseminated rather than localized disease, and are often taking concomitant immunosuppressants such as methotrexate or corticosteroids with HUMIRA.

Treatment with HUMIRA should not be initiated in patients with an active infection, including localized infections. 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;
- 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.

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.

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.

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 In the controlled portions of clinical trials of some TNF-blocking agents, including HUMIRA, more cases of malignancies have been observed among patients receiving those TNF blockers compared to control patients. During the controlled portions of HUMIRA trials in patients with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, and plaque psoriasis, malignancies, other than lymphoma and non-melanoma (basal cell and squamous cell) skin cancer, were observed at a rate (95% confidence interval) of 0.6 (0.3, 1.0)/100 patient-years among 3853 HUMIRA-treated patients versus a rate of 0.4 (0.2, 1.0)/100 patient-years among 2183 control patients (median duration of treatment of 5.5 months for HUMIRA-treated patients and 3.9 months for control-treated patients). The size of the control group and limited duration of the controlled portions of studies precludes the ability to draw firm conclusions. In the controlled and uncontrolled open-label portions of the clinical trials of HUMIRA, the more frequently observed malignancies, other than lymphoma and non-melanoma skin cancer, were breast, colon, prostate, lung, and melanoma. These malignancies in HUMIRA-treated and control-treated patients were similar in type and number to what would be expected in the general population. During the controlled portions of HUMIRA rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, and plaque psoriasis trials, the rate (95% confidence interval) of non-melanoma (basal cell and squamous cell) skin cancers was 0.9 (0.57, 1.35)/100 patient-years among HUMIRA-treated patients and 0.3 (0.08, 0.80)/100 patient-years among control patients. The potential role of TNF blocking therapy in the development of malignancies is not known.

Malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blocking agents (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.

In the controlled portions of clinical trials of all the TNF-blocking agents, more cases of lymphoma have been observed among patients receiving TNF blockers compared to control patients. In controlled trials in patients with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, and plaque psoriasis, 2 lymphomas were observed among 3853 HUMIRA-treated patients versus 1 among 2183 control patients. In combining the controlled and uncontrolled open-label portions of these clinical trials with a median duration of approximately 2 years, including 6539 patients and over 16,000 patient-years of therapy, the observed rate of lymphomas is approximately 0.11/100 patient-years. This is approximately 3-fold higher than expected in the general population. Rates in clinical trials for HUMIRA cannot be compared to rates of clinical trials of other TNF blockers and may not predict the rates observed in a broader patient population. Patients with rheumatoid arthritis, particularly those with highly active disease, are at a higher risk for the development of lymphoma. Cases of acute and chronic leukemia have been reported in association with postmarketing TNF-blocker use in rheumatoid arthritis and other indications. Even in the absence of TNF-blocker therapy, patients with rheumatoid arthritis may be at a higher risk (approximately 2-fold) than the general population for the development of leukemia.

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, 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 *[see Adverse Reactions]*. 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 Serious infections were seen in clinical studies with concurrent use of anakinra (an interleukin-1 antagonist) and another TNF-blocking agent, etanercept, with no added benefit compared to etanercept alone. 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.

Immunosuppression The possibility exists for TNF blocking agents, including HUMIRA, to affect host defenses against infections and malignancies since TNF mediates inflammation and modulates cellular immune responses. The safety and efficacy of HUMIRA in patients with immunosuppression have not been evaluated.

ADVERSE REACTIONS

Clinical Studies Experience The most serious adverse reactions were *[see Warnings and Precautions]*:

- Serious Infections
- Neurologic Reactions
- Malignancies

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 placebo-controlled rheumatoid arthritis trials, the rate of infection was 1 per patient-year in the HUMIRA-treated patients and 0.9 per patient-year in the placebo-treated patients. The infections consisted primarily of upper respiratory tract infections, bronchitis and urinary tract infections. Most patients continued on HUMIRA after the infection resolved. The incidence of serious infections was 0.04 per patient-year in HUMIRA treated patients and 0.02 per patient-year in placebo-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 completed and ongoing global clinical studies that include over 13,000 patients, the overall rate of tuberculosis is approximately 0.26 per 100 patient-years. In over 4500 patients in the US and Canada, the rate is approximately 0.07 per 100 patient-years. These studies include reports of miliary, lymphatic, peritoneal, as well as pulmonary. Most of the cases of tuberculosis occurred within the first eight months after initiation of therapy and may reflect recrudescence of latent disease. Cases of opportunistic infections have also been reported in these clinical trials at an overall rate of approximately 0.075/100 patient-years. Some cases of opportunistic infections and tuberculosis have been fatal *[see Warnings and Precautions]*.

Malignancies More cases of malignancy have been observed in HUMIRA-treated patients compared to control-treated patients in clinical trials *[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.

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 2.6%. The immunogenicity rate was 8% for plaque psoriasis patients who were treated with HUMIRA monotherapy.

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. Adverse reaction rates in patients treated with HUMIRA 40 mg weekly were similar to rates in patients treated with HUMIRA 40 mg every other week. 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)	Percentage	Percentage
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		
Injection site pain	12	12
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 erythema and/or itching, hemorrhage, pain or swelling

Juvenile Idiopathic Arthritis Clinical Studies In general, the adverse reactions in pediatric patients were similar in frequency and type to those seen in adult patients *[see Warnings and Precautions* and other sections under *Adverse Reactions]*. Important findings and differences from adults are discussed in the following paragraphs.

HUMIRA has been studied in 171 pediatric patients, 4 to 17 years of age, with polyarticular juvenile idiopathic arthritis. 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 juvenile idiopathic arthritis patients were generally similar to those commonly seen in outpatient JIA populations. 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 juvenile idiopathic arthritis exposed to HUMIRA alone; liver function tests (LFT) elevations were more frequent among those treated with the combination of HUMIRA and MTX. In general, these elevations did not lead to discontinuation of HUMIRA treatment.

In the juvenile idiopathic arthritis 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 in two placebo-controlled trials and in an open label study and in 393 patients with ankylosing spondylitis in two placebo-controlled studies. The safety profile for patients with psoriatic arthritis and ankylosing spondylitis treated with HUMIRA 40 mg every other week was similar to the safety profile seen in patients with rheumatoid arthritis, HUMIRA Studies RA-I through IV. In the clinical trials of patients with psoriatic arthritis and ankylosing spondylitis, elevations of aminotransferases were observed (ALT more common than AST) in a greater proportion of patients receiving HUMIRA than in controls, both when HUMIRA was given as monotherapy and when it was used in combination with other immunosuppressive agents. Most elevations of ALT and AST observed were in the range of 1.5 to 3 times the upper limit of normal. In general, patients who developed ALT and AST elevations were asymptomatic, and the abnormalities decreased or resolved with either continuation or discontinuation of HUMIRA, or modification of concomitant medications.

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 rheumatoid arthritis.

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 rheumatoid arthritis 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%).

Elevations of aminotransferases were observed (ALT more common than AST) in a greater proportion of patients receiving HUMIRA than in controls. Most elevations of ALT and AST observed were in the range of 1.5 to 3 times the upper limit of normal. In general, patients who developed ALT and AST elevations were asymptomatic, and most of the abnormalities decreased or resolved with either continuation or discontinuation of HUMIRA.

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.

Hematologic reactions: Thrombocytopenia *[see Warnings and Precautions]*

Hypersensitivity reactions: Anaphylaxis, angioneurotic edema *[see Warnings and Precautions]*

Respiratory disorders: Interstitial lung disease, including pulmonary fibrosis

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

DRUG INTERACTIONS

Anakinra Concurrent administration of anakinra (an interleukin-1 antagonist) and another TNF-blocking agent has been associated with an increased risk of serious infections, an increased risk of neutropenia and no additional benefit compared to these medicinal products alone. Therefore, the combination of anakinra with other TNF-blocking agents, including HUMIRA, may also result in similar toxicities *[see Warnings and Precautions]*.

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

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

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 have not been established.

Juvenile Idiopathic Arthritis In the juvenile idiopathic arthritis study, HUMIRA was shown to reduce signs and symptoms of active polyarticular juvenile idiopathic arthritis 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.

Safety of HUMIRA in pediatric patients was generally similar to that observed in adults with certain exceptions *[see Adverse Reactions]*.

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

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.

- **Immunosuppression** Inform patients that HUMIRA may lower the ability of their immune system to fight infections. Instruct the patient of the importance of contacting their doctor if they develop any symptoms of infection, including tuberculosis and reactivation of hepatitis B virus infections.
  Patients should be counseled about the risk of lymphoma and other 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 heart disease, neurological disease, or autoimmune disorders. Advise patients to report any symptoms suggestive of a cytopenia such as bruising, bleeding, or persistent fever.

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Faces of Premier

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

Johanna Forlivio, RPA-C *(left)*
Physician Assistant, GI Associates

Kevin Torrens, RPA-C *(center)*
Physician Assistant, Hudson Valley Urology

H. Janelle Carr, FNP-BC *(right)*
Nurse Practitioner, GI Associates

Highly trained, licensed and certified, the physician assistants and nurse practitioner at Premier Medical are crucial members of your healthcare team.

Typically, PAs and NPs are utilized to take medical histories, perform exams and procedures, order and interpret diagnostic tests, diagnose illnesses, and prescribe medication. The medical professionals at Premier Medical do all that, and more… they provide a continuity of care that contributes greatly to the comfort and safety of our patients.

"Johanna and I both take care of GI Associates' patients when they're in the hospital," says Janelle. "We see them every day, order their diagnostic tests and review the lab work. We're there when patients come into the emergency room with an acute problem, and we're on duty from 8 a.m. to 'whenever'."

At Hudson Valley Urology, Kevin is often a "portal" into the practice. Besides hospital rounds, his duties include making sure, no matter how busy the physicians may be, there's always someone knowledgeable available to put a patient on the path to treatment. "If patients wish to, they can stay with me for care," says Kevin. "But for things that need more advanced diagnosis or treatment, they'll be connected to the appropriate physician right away.

"Everyone is facing a challenge when they come to the doctor," he observes. "It's great to put patients at ease by explaining the processes, the why and wherefore."