SUMMER 2012



# The Rocky Mountain

Rocky Mountain Hemophilia & Bleeding Disorders Association

*RMHBDA is a 501(c)(3) nonprofit organization founded in 2000 and is a chartered chapter of the National Hemophilia Foundation.*

*Our mission is to improve the quality of care and life for persons with inherited bleeding disorders, including hemophilia and von Willebrand Disease through education, peer support, resources, and referral.*

## In This Issue




**Rocky Mountain Hemophilia & Bleeding Disorders Association**

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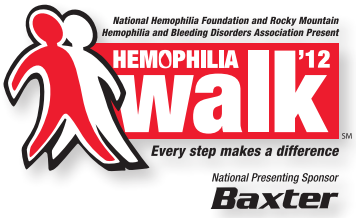
## RMHBDA Family Camp 2012
### A Great Success

Our annual family camp would not be possible without our generous program funders: Accredo Health, Inc., Baxter, Biogen Idec, CSL Behring, Grifols, Novo Nordisk, Pfizer, Restore RX, The Gilhousen Family Foundation, and Walgreens Infusion Services.

RMHBDA Family camp was held June 22–24, 2012 at the Bear Lodge Resort in the Big Horn National Forrest in Wyoming, with 16 families attending comprised of 24 youth and 41 adults. Thank you to all who

*Continued on page 2*

## First Annual Walk for Hemophilia!




Join us for our first Annual Montana and Wyoming Walk for Hemophilia!

### Save the Date

**September 8, 2012**
**Bogert Park, Bozeman, Montana**
**Registration begins at 9:30 A.M.**
**Walk starts at 11:00 A.M.**

### Create or Join a Walk Team

Visit www.hemophilia.org/walk and click on the "MT" link, then click on your preference: "Register," "Donate," "Create a team," or "Join a Team."

### Can't Make It? We Understand!

But you can still participate and contribute by hosting a "mini walk," a BBQ, a small party, or an event in your community, or search out "virtual walkers" who can't

*Continued on page 5*

## National Hemophilia Foundation Annual Meeting



Start planning now for the National Hemophilia Foundation's 64th Annual Meeting, "Mapping Our Future," in Orlando, Florida, November 8–10, 2012. Florida is one of our most popular destinations, as many attendees extend their visits to vacation in Orlando, taking in all the city has to offer.


During our yearly three-day gathering, you can be sure we will keep you busy, with educational sessions to attend, networking opportunities with others experiencing

*Continued on page 3*

## From Our Board President

*Summer has finally arrived and each year this season seems to get busier and busier as I dream of sandy beaches, forests, a cool beverage, and time with family. This year is no exception.*

*Summer was kicked off in style at Camp Big Sky in beautiful Wyoming. Thank you to the camp committee of Jessica, Andrea, and Sue! A huge thank you to the Stafford and Scott families for the time and energy spent on the most delicious food. It was truly a feast for every meal. Finally, thank you to all the families and sponsors that made this event successful.*

*With the Affordable Health Care Act upheld by the Supreme Court, we now must be aware of what Montana and Wyoming will have in place. Please contact me if you would like to be part of the advocacy team.*

*The Walk is around the corner and if you have not done so, please register your team on the website. With people enjoying the great outdoors, now is good time to fund raise through e-mail. With everyone's help, we will be successful.*

*Enjoy the summer and family time this season brings. May everyone be safe in their travels and will see you in Bozeman on September 8th for our Walk.*

*Respectfully,*
*Lisa Maxwell,*
*President RMHBDA, 3lisamaxwell@gmail.com, 406.788.0843*

 *Designed by & masthead photo courtesy of Fifth Street Design, Bozeman, Montana.*


## Family Camp *(continued from page 1)*

attended, and for participating in the Friday night potluck.

Adults and youth ages 10–17 participated in a powerfully engaging program presented by Pat Torrey, his program was an inspiration to all who attended.

Children ages 2–10 enjoyed numerous arts and crafts projects, games, swimming, fishing, building forts in the woods, supported by Amanda and Kristine of Pat Torrey's staff.

Thank you to the camp committee and our chapter volunteers: Sue Scott, Andrea & Leroy Stafford, Bailey, Dan, Becky, and Lisa Stafford, Jessica Amende, and Lisa Maxwell!

*Your good work and valuable time made family camp a wonderful experience for everyone!*


## National Hemophilia Foundation Annual Meeting *(continued from page 1)*

similar issues, and social events that help you unwind. The Activity Program for Kids & Teens will be taking a field trip to SeaWorld Orlando to enjoy thrilling rides, educational exhibits, animal shows and a chance to see everybody's favorite killer whale, Shamu. Universal Studios Orlando will open its gate for our Final Night Event. What could be more fun than a theme park at night?

**A sneak preview of sessions includes:**

- "It's a Guy Thing, Too: Men with von Willebrand Disease"
- " 'I Don't Need a Support Group — I have Facebook!' Risks and Rewards of Life Online"
- "The Glass is Half Full: Reframing Emotional Challenges for Women"
- "Head, Shoulders, Knees and Toes! Exploring the Pros and Cons of Protection Devices, such as MedicAlert, Pads and Helmets."

Once again, NHF will host a two-day Medical Track for Researchers and Physicians. One of the highlights of that meeting is a poster abstract presentation and reception. Separate tracks for nurses, physical therapists and social workers will provide sessions on inhibitors, sports participation and the role of social workers in genetics, respectively.


## Inhibitor Education Summits Welcome Patients and Their Families

### There will be four educational conferences this year

Reprinted with the permission of the National Hemophilia Foundation

*By Beth Marshall | 04.13.2012*

Registration is now open for the National Hemophilia Foundation's (NHF's) 2012 Inhibitor Education Summits, educational conferences for people who have hemophilia with inhibitors and their families. There will be four educational conferences this year.

Two of the summits are for Spanish-speaking families, in Los Angeles on May 11–13, and in Miami on June 22–24. The other two summits in English will take place in Miami on July 19–22, and in San Diego on August 2–5. The Inhibitor Education Summits are made possible by an educational grant from Novo Nordisk. They are open to first-time and repeat attendees. Childcare is available at all summits for children up to age 12.

In some people with hemophilia, the immune system reacts to the recombinant clotting factor by perceiving it as foreign and creating antibodies called inhibitors. Inhibitors combat the clotting factor, rendering it ineffective in treating bleeds. Between 10% and 30% of people with hemophilia A and 1%–4% of people with hemophilia B develop inhibitors.

Having a complication from an already-rare disorder can make life difficult for people with hemophilia with inhibitors and their families. Their experiences of treatments and bleeds are so different from people for whom recombinant factor works as it should. The sessions at the summits are designed to meet the health and emotional needs of this population, and were created by a committee of doctors, nurses, physical therapists and social workers who have experience treating people who have hemophilia with inhibitors.

Each English inhibitor summit is divided into four tracks:

- "Hemophilia With Inhibitors 101," for people who are newly diagnosed;
- "Hemophilia 201," an intermediate track;
- "Young Men With Inhibitors (16–19)," for teenagers with inhibitors and their siblings; and
- "Adult Men With Inhibitors (19 and Beyond)," for adult men.

Both the English and Spanish summits will offer sessions on new drugs in development, tips for parents, sports and exercise, and immune tolerance therapy.

Travel and accommodation assistance is available to all eligible attendees. Get more information about registering by visiting www.nhfinhibitorsummits.org.

## New & Great Things Are Happening at RMHBDA!

### Facebook

Join our new Facebook page before July 29 to have your name entered for a prize drawing!

www.facebook.com/**rmhbda**

### New Website

Check out our amazing new website, www.rockymountainhemophilia.org.

I welcome your feedback and input, it's your organization!

### Questions & Feedback

Contact Brad at 406.600.2554 or brad.rmhbda@gmail.com.

## Six New Stem Cell Lines Now Publicly Available

*ScienceDaily (June 14, 2012)* — **Six new human embryonic stem cell lines derived at the University of Michigan have just been placed on the U.S. National Institutes of Health's registry, making the cells available for federally-funded research.**

U-M now has a total of eight cell lines on the registry, including five that carry genetic mutations for serious diseases such as the severe bleeding disorder hemophilia B, the fatal brain disorder Huntington's disease and the heart condition called hypertrophic cardiomyopathy, which causes sudden death in athletes and others.

Researchers at U-M and around the country can now begin using the stem cell lines to study the origins of these diseases and potential treatments. Two of the cell lines are believed to be the first in the world bearing that particular disease gene.

The three U-M stem cell lines now in the registry that do not carry disease genes are also useful for general studies and as comparisons for stem cells with disease genes. In all, there are 163 stem cell lines in the federal registry, most of them without major disease genes.

Each of the lines was derived from a cluster of about 30 cells removed from a donated five-day-old embryo roughly the size of the period at the end of this sentence. The embryos carrying disease genes were created for reproductive purposes, tested and found to be affected with a genetic disorder, deemed not suitable for implantation and would have otherwise been discarded if not donated by the couples who donated them.

Some came from couples having fertility treatment at U-M's Center for Reproductive Medicine, others from as far away as Portland, OR. Some were never frozen, which may mean that the stem cells will have unique characteristics and utilities.

The full list of U-M-derived stem cell lines accepted to the NIH registry includes:

- UM9-1PGD — Hemophilia B UM17-1 PGD – Huntington's disease
- UM38-2 PGD — Hypertrophic Cardiomyopathy (MYBPC3)
- UM15-4 PGD — Hydroxysteroid Dehydrogenase 4 Deficiency, a rare hormone disorder
- UM11-1PGD — Charcot-Marie-Tooth disease Type 1A
- UM4-6 — no disease gene
- UM14-1 — no disease gene
- UM14-2 — no disease gene

"Our last three years of work have really begun to pay off, paving the way for scientists worldwide to make novel discoveries that will benefit human health in the near future," says Gary Smith, Ph.D., who derived the lines and also is co-director of the U-M Consortium for Stem Cell Therapies, part of the A. Alfred Taubman Medical Research Institute.

"Each cell line accepted to the registry demonstrates our attention to details of proper oversight, consenting, and following of NIH guidelines," says Sue O'Shea, Ph.D., professor of Cell and Developmental Biology at the U-M Medical School, and co-director of the Consortium for Stem Cell Therapies.

"U-M is one of only three academic institutions to have disease-specific stem cell lines listed in the national registry," says Smith, who is a professor in the Department of Obstetrics and Gynecology at the University of Michigan Medical School. The first line, a genetically normal one, was accepted to the registry in February.

Each line is the culmination of years of preparation and cooperation between U-M and Genesis Genetics, a Michigan-based genetic diagnostic company. This work was made possible by Michigan voters' November 2008 approval of a state constitutional amendment permitting scientists to derive embryonic stem cell lines using surplus embryos from fertility clinics or embryos with genetic abnormalities and not suitable for implantation.

The amendment also made possible an unusual collaboration that has blossomed between the University of Michigan and molecular research scientists at Genesis Genetics, a company that has grown in only eight years to become the leading global provider of pre-implantation genetic diagnosis (PGD) testing. PGD is a testing method used to identify embryos carrying the genetic mutations responsible for serious inherited diseases.

*Gary Smith removes a rack containing vials that hold frozen human embryos donated to the U-M Consortium for Stem Cell Therapies.* [University of Michigan photo]

Genesis Genetics performs nearly 7,500 PGD tests annually. Under the arrangement between the company and U-M, patients with embryos that test positive for a genetic disease now have the option of donating those embryos to U-M if they have decided not to use them for reproductive purposes and the embryos would otherwise be discarded.

The agreement was worked out between U-M's Smith and Mark Hughes, M.D., Ph.D., founder and president of Genesis Genetics and a pioneer in the field of pre-implantation genetic diagnosis. "These are very precious cells, and it would be unconscionable not to take advantage of such an opportunity for medical science and the cure of disease," Hughes says.

The hemophilia B line also resulted from a collaboration with the Oregon Health Science University, and is believed to be the first of its kind in the world. Through the partnership with the Reproductive Endocrinology and Infertility division, headed by Philip Patton, M.D., and the work of David Battaglia, Ph.D., the single embryo was frozen at OHSU and shipped to Michigan.

Contributors to the A. Alfred Taubman Medical Research Institute's Consortium for Stem Cell Therapies include the Taubman Institute; the Office of the Executive Vice President for Medical Affairs; the Office of the Medical School Dean; the Comprehensive Cancer Center; the Department of Pediatrics and Communicable Diseases; the Office of the Vice President for Research; the School of Dentistry; the Department of Pathology; the Department of Cell and Developmental Biology; the College of Engineering; the Life Sciences Institute; the Department of Neurology; and U-M's Michigan Institute for Clinical and Health Research.

## About RMHBDA

We are a chapter of the National Hemophilia Foundation. RMHBDA was founded in 2000, as a 501(c)(3) nonprofit service and consumer advocacy organization to support and educate those affected by and involved in the treatment of bleeding disorders. We work throughout Montana and Wyoming, where there are currently no disease-specific treatment centers.

Rocky Mountain Hemophilia & Bleeding Disorders Association

Our mission is to improve the quality of care and life for persons with inherited bleeding disorders, including hemophilia and von Willebrand Disease (VWD), through education, peer support, resources, and referral.

### What We Do

- Legislative lobbying at the national and state level
- Family Camp and Mile High Camp
- Patient Assistance
- Educational Scholarships
- Community Education
- Fundraisers: Raffle, Annual MT & WY Walk for Hemophilia
- Monitoring of health issues with federal and state agencies, and other non-profit organizations

### RMHBDA Board of Directors

- Lisa Maxwell, Great Falls, MT, *President*
- Forrest Berg, Bozeman, MT, *Treasurer*
- Jane Robertson, Cody, WY, *Secretary*
- Kyrsten Brinkley, Missoula, MT
- Jim Ferriter, Helena, MT
- Chris Graham, Billings, MT
- Spencer Straub, Cheyenne, WY
- Sean Jeffrey, Missoula, MT

### Staff

- Brad Benne, Executive Director
- Sara Jestrab, Summer Intern

### RMHBDA Contact Info

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www.rockymountainhemophilia.org • brad.rmhbda@gmail.com

**This is your organization!** Please let us know how we are doing!

### IRS Identification

- Tax ID #81-0533720

### Volunteer Opportunities!

If you are interested in volunteering in events, activities, special committees or donating your valuable time, then please contact Brad Benne. Your involvement and support are greatly appreciated!

## Former NHF Education Manager & Project Red Flag Director Dies

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Anna DeSimone, former Education Manager and Director of the National Hemophilia Foundation's (NHF) Project Red Flag, died on Thursday, April 19, 2012, of complications from myelofibrosis, a bone marrow disorder. She was 61.

DeSimone became involved in the bleeding disorders community after her son was born with hemophilia in the late 1980s. She joined her local chapter, the Hemophilia Association of New Jersey, where she eventually became a trustee, then president of the board.

From 2003-2008 DeSimone worked at NHF. She was hired as Coordinator of Project Red Flag, a national awareness campaign for women with von Willebrand disease and other bleeding disorders. She then became director of the program. In that position she helped created a checklist for school nurses and sessions at NHF's Annual Meetings for women with bleeding disorders. She also met with NHF chapters to help them strengthen their programming for women. In 2004 DeSimone was appointed by the governor of New Jersey to serve on a Task Force on Women and Bleeding Disorders.

DeSimone served on the board of the Hemophilia Federation of America. She was a founding board member and treasurer of the Foundation for Women & Girls with Blood Disorders, a nonprofit organization providing information for healthcare providers.

DeSimone will be remembered as an activist and educator, a champion for the needs of women with bleeding disorders. She is survived by her husband and two children.

### First Annual Walk for Hemophilia! *(continued from page 1)*

attend as well! Tell them they can, "sleep in, save gas, and get a t-shirt," and still make a big difference for your family and families throughout Montana and Wyoming.

Please consider talking with Brad Benne about how you can help! Your support is appreciated, this is your organization!

National Hemophilia Foundation and Rocky Mountain Hemophilia and Bleeding Disorders Association Present
HEMOPHILIA walk '12
Every step makes a difference
National Presenting Sponsor Baxter

## As I See It

Cazandra Campos-MacDonald



# Day and Night: Hemophilia the Second Time Around

My boys are like day and night. My 15-year-old, Julian, is a free spirit: creative, artistic, a great sense of humor, and a gifted musician. His idea of a perfect day is to be in New York City watching Broadway shows. My 5-year-old, Caeleb, adores choo-choo trains and playing in the dirt, can't get enough chocolate ice cream, and embraces life with all his heart. They have a bond as brothers, and they also share the bond of severe hemophilia A.

Julian was almost 10 when Caeleb was born. When my husband Joe and I broke the news to Julian that his little brother also had hemophilia, he clapped and jumped for joy! We were stunned. Why was he so excited? "When I am in leadership training at camp," Julian replied, "he will be a camper!" My sweet son saw only the commonalities and blessings of hemophilia. He would share one of his most exciting summer activities with his baby brother.

*Follow more of her journey with hemophilia: 2brotherswithhemophilia.blogspot.com*

But my boys don't share everything. Caeleb wants to go to a monster truck rally, and Julian loves watching live theater. Caeleb is a social butterfly, while Julian keeps to himself. And as for hemophilia, they can't even begin to compare adventures.

Julian's hemophilia has been pretty easy so far. No major bleeds or target joints, and a port that lasted five years without infection. Caeleb, on the other hand, has a target joint and suffers from extremely painful bleeds. He is on his fourth port, fights a high-titer inhibitor, and has been hospitalized often. With ten years' difference between my boys, at times I still feel like a "newly diagnosed" parent.

During one of Caeleb's hospital stays, the nurses were having a tough time starting an IV. Poke after poke, nurse after nurse, and my Julian, 12 at the time, was standing outside the room crying silent tears for his brother. His knowledge of empathy and compassion will always be with him. He loves deeply. As for Caeleb, when he has an infusion or blood draw peripherally, despite his fear, he tries his hardest not to "cry and wiggle," so he can "be like his big bro."

My sons and their hemophilia differ significantly—you'd almost think they have different severity levels and even different bleeding disorders. But a medical condition may manifest in its own way in each person: what is day to one becomes night to another. Over the past five years, our family has spent immense time and energy learning to live with Caeleb's hemophilia. It's been challenging, compared to the ten years before Caeleb's birth, but one thing's for sure: my boys struggle with their bleeding disorder in different ways, and it has bonded them together.

In 2010, while I was out of town, Caeleb's port was not working and my husband had to access him peripherally. Caeleb was having an active bleed, and infusing him was an emergency; we live two hours from the hemophilia treatment center. Instead of letting his little brother be uncomfortable and scared, Julian sat with him, explained what was going to happen, and never stopped holding his hand. His encouragement helped my husband focus on the actual infusion instead of having to keep Caeleb calm. My husband never prompted Julian to help. Julian just rose to the occasion and did what brothers do.

No one chooses to have a chronic illness. It just happens. Hemophilia has changed my family—it has brought out the best in us all. My husband and I are closer than ever in our 22 years together. The reality of hemophilia can damage and destroy relationships, but luckily, we have made it through stronger than before. Of course, if I could banish hemophilia, I would in a second! And yet, I have so many blessings in my life that if I could give them away, it would be by the truckload. I hope that when I share my story or a few words of encouragement, someone may see a positive in what's often the negative of living with a chronic condition.

Siblings can be like day and night. One is the life of the party, and the other prefers a quiet corner. One is a sports nut, and the other a musician. One is a math whiz, and the other a writer. I had no idea, when hemophilia came into my life a second time, that this journey would be so incredibly different from the first. Ten years after my older son was born, my younger son's birth has become the biggest surprise and biggest challenge of my life.

But day always follows night, and dawn brings hope. Hope can be the best of things, and it never abandons you. I am filled with hope that my sons will continue to thrive despite their bleeding disorder. I am filled with hope that my husband and I will gather the strength and knowledge we need to continue managing Julian's and Caeleb's treatments. And I am filled with hope that one day, the light will reveal itself and we will move into another, even better season while living with hemophilia.

*Cazandra lives in Truth or Consequences, NewMexico, with her husband, Joe, and their sons, Julian and Caeleb. She works in the healthcare industry, is active in church ministry, and writes a column for the local newspaper.*

## WFH appoints John E. Bournas as new CEO/Executive Director



The World Federation of Hemophilia (WFH) is pleased to announce the appointment of John E. Bournas as CEO/Executive Director. Bournas brings over fifteen years of senior managerial experience in the healthcare and not-for-profit sectors and international experience as a diplomat. His areas of expertise include management, business development, healthcare advocacy, and cultivating relationships with stakeholders at the highest level of government. Bournas started his new position on January 25.

"The WFH is delighted to welcome John Bournas to our team," said WFH president Mark W. Skinner. "He brings a unique combination of skills and an international perspective that will be integral to achieving our strategic goals in the coming years."

Prior to joining the WFH, Bournas was senior director of international affairs with the American College of Cardiology Foundation, the largest international professional society for cardiologists. He was responsible for global strategic planning, international memberships, partnering with national healthcare societies, global advocacy, and diversifying the organization's revenue stream through engagement with its corporate partners. Before that, Bournas was senior director-international with Cardinal Health in the United States, a Fortune 19 company that specialized in improving the cost-effectiveness of health care.

Bournas has also worked and travelled throughout the world developing relationships and bridging gaps between developed and developing countries. He worked as a diplomat in Chile, Australia, and Japan, overseeing international trade and development projects. The son of Chilean and Greek parents, he was raised in Chile and the United States. He speaks Spanish, French, Portuguese, and some Japanese and Greek.

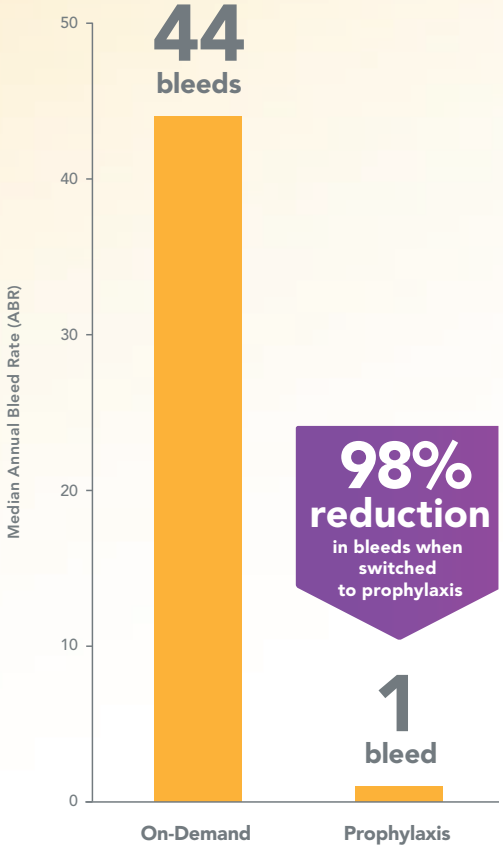
Bournas holds a Master of Business Administration degree from Macquarie University in Australia, a Master of Arts in Political Science from Fordham University in the United States, and a Bachelor of Arts in International Studies from Fairleigh Dickinson University in the United States. He is married and has four children.

Prophylaxis with ADVATE delivers 44 to 1[1]

**ADVATE** IS THE **ONLY** RECOMBINANT FACTOR VIII (EIGHT) THAT IS


PROPHYLAXIS WITH ADVATE

# THE POWER TO REDUCE YOUR ANNUAL BLEED RATE (ABR)




## Significant reduction in ABR[1]

After switching from 6 months of on-demand treatment to 12 months of prophylaxis with ADVATE in 53 previously treated patients with severe or moderately severe hemophilia A:

- **Median ABR of 1** while on either prophylaxis regimen[1]
  - prophylaxis every second day (20-40 IU/kg)
  - prophylaxis every third day (20-80 IU/kg, targeted to maintain FVIII trough levels ≥1%)
- **42% of patients experienced zero bleeds** during 1 year on prophylaxis[1]
- **No subject developed factor VIII inhibitors** or withdrew due to an adverse event (AE)[4]

## Indication for ADVATE

ADVATE [Antihemophilic Factor (Recombinant), Plasma/Albumin-Free Method] is a medicine used to replace clotting factor VIII that is missing in people with hemophilia A (also called "classic" hemophilia). ADVATE is used to prevent and control bleeding in people with hemophilia A. Your healthcare provider may give you ADVATE when you have surgery.

ADVATE is not used to treat von Willebrand Disease.

**You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.**

**References: 1.** ADVATE prescribing information. Westlake Village, CA: Baxter Healthcare Corporation; December 2011. **2.** Helixate FS prescribing information. Kankakee, IL: CSL Behring LLC; August 2009. **3.** Kogenate FS prescribing information. Tarrytown, NY: Bayer Healthcare LLC; March 2011. **4.** Valentino LA, Mamonov V, Hellmann A, et al. A randomized comparison of two prophylaxis regimens and a paired comparison of on-demand and prophylaxis treatments in hemophilia A management. *J Thromb Haemost.* 2012;10(3):359-367. **5.** Maruish ME, ed. *User's Manual for the SF-36v2 Health Survey.* 3rd ed. Lincoln, RI: QualityMetric Incorporated; 2011.



**TALK TO YOUR HEALTHCARE PROVIDER TO SEE HOW PROPHYLAXIS**

FDA APPROVED FOR PROPHYLAXIS IN BOTH **ADULTS & CHILDREN (0-16 YEARS)**[1-3]

**PROPHYLAXIS WITH ADVATE**

# THE POWER TO IMPROVE YOUR PHYSICAL HEALTH–RELATED QUALITY OF LIFE


**Physical Component Score**

Improvements in physical functioning, well-being, and energy level.[5]

**Bodily Pain**

Reduced levels of pain and improvements in the limitations of work due to pain.[5]

**Role Physical**

Improvements in the ability to perform physical activities without limitations due to health.[5]

## Clinically meaningful improvements

**After 12 months of prophylactic treatment**, physical health–related quality of life improved in patients, mainly due to clinically meaningful improvements in*:

- the amount of pain experienced by a patient and how much pain interferes with normal work
- the impact physical health can have on performing work or other daily activities

*Clinically significant changes were not seen in the physical health–related sub-categories of General Health and Physical Functioning and the mental health–related component score and sub-categories of Mental Health, Role Emotional, Social Functioning, and Vitality.

## Detailed Important Risk Information for ADVATE

You should not use ADVATE if you are allergic to mice or hamsters or any ingredients in ADVATE.

You should tell your healthcare provider if you have or have had any medical problems, take any medicines, including prescription and non-prescription medicines and dietary supplements, have any allergies, including allergies to mice or hamsters, are nursing, are pregnant, or have been told that you have inhibitors to factor VIII.

You can have an allergic reaction to ADVATE. Call your healthcare provider right away and stop treatment if you get a rash or hives, itching, tightness of the throat, chest pain or tightness, difficulty breathing, lightheadedness, dizziness, nausea, or fainting.

Your body may form inhibitors to factor VIII. An inhibitor is part of the body's normal defense system. If you form inhibitors, it may stop ADVATE from working properly. Consult with your healthcare provider to make sure you are carefully monitored with blood tests for the development of inhibitors to factor VIII.

Side effects that have been reported with ADVATE include: cough, sore throat, unusual taste, abdominal pain, diarrhea, nausea/vomiting, headache, fever, dizziness, hot flashes, chills, sweating, joint swelling/aching, itching, hematoma, swelling of legs, runny nose/congestion, and rash.

Call your healthcare provider right away about any side effects that bother you or if your bleeding does not stop after taking ADVATE.

**Please see Brief Summary of ADVATE Prescribing Information on the next page.**

ADVATE
[Antihemophilic Factor (Recombinant), Plasma/Albumin-Free Method]

There's more to life.

**advate.com | 888.4.ADVATE**

**WITH ADVATE CAN HELP REDUCE YOUR ANNUAL BLEED RATE (ABR)**

# ADVATE
# [Antihemophilic Factor (Recombinant), Plasma/Albumin-Free Method]
## Brief Summary of Prescribing Information. Please see package insert for full prescribing information.

## INDICATIONS AND USAGE

### Control and Prevention of Bleeding Episodes

ADVATE [Antihemophilic Factor (Recombinant), Plasma/Albumin-Free Method] is an Antihemophilic Factor (Recombinant) indicated for control and prevention of bleeding episodes in adults and children (0-16 years) with Hemophilia A.

### Perioperative Management

ADVATE is indicated in the perioperative management in adults and children (0-16 years) with Hemophilia A.

### Routine Prophylaxis

ADVATE is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and children (0-16 years) with Hemophilia A.

ADVATE is not indicated for the treatment of von Willebrand disease.

## CONTRAINDICATIONS

Known anaphylaxis to mouse or hamster protein or other constituents of the product.

## WARNINGS AND PRECAUTIONS

### Anaphylaxis and Hypersensitivity Reactions

Allergic-type hypersensitivity reactions, including anaphylaxis, are possible and have been reported with ADVATE. Symptoms have manifested as dizziness, paresthesias, rash, flushing, face swelling, urticaria, dyspnea, and pruritus. [See Patient Counseling Information (17) in full prescribing informaiton]

ADVATE contains trace amounts of mouse immunoglobulin G (MuIgG): maximum of 0.1 ng/IU ADVATE and hamster proteins: maximum of 1.5 ng/IU ADVATE. Patients treated with this product may develop hypersensitivity to these non-human mammalian proteins.

Discontinue ADVATE if hypersensitivity symptoms occur and administer appropriate emergency treatment.

### Neutralizing Antibodies

Carefully monitor patients treated with AHF products for the development of Factor VIII inhibitors by appropriate clinical observations and laboratory tests. Inhibitors have been reported following administration of ADVATE predominantly in previously untreated patients (PUPs) and previously minimally treated patients (MTPs). If expected plasma Factor VIII activity levels are not attained, or if bleeding is not controlled with an expected dose, perform an assay that measures Factor VIII inhibitor concentration. [See Warnings and Precautions, Monitoring Laboratory Tests]

### Monitoring Laboratory Tests

The clinical response to ADVATE may vary. If bleeding is not controlled with the recommended dose, determine the plasma level of Factor VIII and administer a sufficient dose of ADVATE to achieve a satisfactory clinical response. If the patient's plasma Factor VIII level fails to increase as expected or if bleeding is not controlled after the expected dose, suspect the presence of an inhibitor (neutralizing antibodies) and perform appropriate tests as follows:

- Monitor plasma Factor VIII activity levels by the one-stage clotting assay to confirm the adequate Factor VIII levels have been achieved and maintained when clinically indicated. [See Dosage and Administration (2) in full prescribing information]
- Perform the Bethesda assay to determine if Factor VIII inhibitor is present. If expected Factor VIII activity plasma levels are not attained, or if bleeding is not controlled with the expected dose of ADVATE, use Bethesda Units (BU) to titer inhibitors.
  - If the inhibitor titer is less than 10 BU per mL, the administration of additional Antihemophilic Factor concentrate may neutralize the inhibitor and may permit an appropriate hemostatic response.
  - If the inhibitor titer is above 10 BU per mL, adequate hemostasis may not be achieved. The inhibitor titer may rise following ADVATE infusion as a result of an anamnestic response to Factor VIII. The treatment or prevention of bleeding in such patients requires the use of alternative therapeutic approaches and agents.

## ADVERSE REACTIONS

The serious adverse drug reactions (ADRs) seen with ADVATE are hypersensitivity reactions and the development of high-titer inhibitors necessitating alternative treatments to Factor VIII.

The most common ADRs observed in clinical trials (frequency ≥ 10% of subjects) were pyrexia, headache, cough, nasopharyngitis, vomiting, arthralgia, and limb injury.

### Clinical Trial 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 clinical trials of another drug and may not reflect the rates observed in clinical practice.

ADVATE has been evaluated in five completed studies in previously treated patients (PTPs) and one ongoing study in previously untreated patients (PUPs) with severe to moderately severe Hemophilia A (Factor VIII ≤ 2% of normal). A total of 234 subjects have been treated with ADVATE as of March 2006. Total exposure to ADVATE was 44,926 infusions. The median duration of participation per subject was 370.5 (range: 1 to 1,256) days and the median number of exposure days to ADVATE per subject was 128.0 (range: 1 to 598).[1]

The summary of adverse reactions (ADRs) with a frequency ≥ 5% (defined as adverse events occurring within 24 hours of infusion or any event causally related occurring within study period) is shown in Table 1.

No subject was withdrawn from a study due to an ADR. There were no deaths in any of the clinical studies.

#### IMMUNOGENICITY

The development of Factor VIII inhibitors with the use of ADVATE was evaluated in clinical studies with pediatric PTPs (< 6 years of age with > 50 Factor VIII exposures) and PTPs (≥ 10 years of age with > 150 Factor VIII exposures). Of 198 subjects who were treated for at least 10 exposure days or on study for a minimum of 120 days, 1 adult developed a low-titer inhibitor (2.0 [BU] in the Bethesda assay) after 26 exposure days. Eight weeks later, the inhibitor was no longer detectable, and *in vivo* recovery was normal at 1 and 3 hours after infusion of another marketed recombinant Factor VIII concentrate. This single event results in a Factor VIII inhibitor frequency in PTPs of 0.51% (95% CI of 0.03 and 2.91% for the risk of any Factor VIII inhibitor development).[1,2] No Factor VIII inhibitors were detected in the 53 treated pediatric PTPs.

In clinical studies that enrolled previously untreated subjects (defined as having had up to 3 exposures to a Factor VIII product at the time of enrollment), 5 (20%) of 25 subjects who received ADVATE developed inhibitors to Factor VIII.[1] Four patients developed high titer (> 5 BU) and one patient developed low-titer inhibitors. Inhibitors were detected at a median of 11 exposure days (range 7 to 13 exposure days) to investigational product.

Immunogenicity also was evaluated by measuring the development of antibodies to heterologous proteins. 182 treated subjects were assessed for anti-Chinese hamster ovary (CHO) cell protein antibodies. Of these patients, 3 showed an upward trend in antibody titer over time and 4 showed repeated but transient elevations of antibodies. 182 treated subjects were assessed for mulgG protein antibodies. Of these, 10 showed an upward trend in anti-mulgG antibody titer over time and 2 showed repeated but transient elevations of antibodies. Four subjects who demonstrated antibody elevations reported isolated events of urticaria, pruritus, rash, and slightly elevated eosinophil counts. All of these subjects had numerous repeat exposures to the study product without recurrence of the events and a causal relationship between the antibody findings and these clinical events has not been established.

Of the 181 subjects who were treated and assessed for the presence of anti-human von Willebrand Factor (VWF) antibodies, none displayed laboratory evidence indicative of a positive serologic response.

### Post-Marketing Experience

The following adverse reactions have been identified during post-approval use of ADVATE. 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.

Among patients treated with ADVATE, cases of serious allergic/hypersensitivity reactions including anaphylaxis have been reported and Factor VIII inhibitor formation (observed predominantly in PUPs). Table 2 represents the most frequently reported post-marketing adverse reactions as MedDRA Preferred Terms.

**Table 1**
**Summary of Adverse Reactions (ADRs)[a] with a Frequency ≥ 5% in 234 Treated Subjects[b]**

| MedDRA[c] System Organ Class | MedDRA Preferred Term | Number of ADRs | Number of Subjects | Percent of Subjects |
|---|---|---|---|---|
| General disorders and administration site conditions | Pyrexia | 78 | 50 | 21 |
| Nervous system disorders | Headache | 104 | 49 | 21 |
| Respiratory, thoracic and mediastinal disorders | Cough | 75 | 44 | 19 |
| Infections and infestations | Nasopharyngitis | 61 | 40 | 17 |
| Gastrointestinal disorders | Vomiting | 35 | 27 | 12 |
| Musculoskeletal and connective tissue disorders | Arthralgia | 44 | 27 | 12 |
| Injury, poisoning and procedural complications | Limb injury | 55 | 24 | 10 |
| Infections and infestations | Upper respiratory tract infection | 24 | 20 | 9 |
| Respiratory, thoracic and mediastinal disorders | Pharyngolaryngeal pain | 23 | 20 | 9 |
| Respiratory, thoracic and mediastinal disorders | Nasal congestion | 24 | 19 | 8 |
| Gastrointestinal disorders | Diarrhea | 24 | 18 | 8 |
| Gastrointestinal disorders | Nausea | 21 | 17 | 8 |
| General disorders and administration site conditions | Pain | 19 | 17 | 8 |
| Skin and subcutaneous tissue disorders | Rash | 16 | 13 | 6 |
| Infections and infestations | Ear infection | 16 | 12 | 5 |
| Injury, poisoning and procedural complications | Procedural pain | 16 | 12 | 5 |
| Respiratory, thoracic and mediastinal disorders | Rhinorrhea | 15 | 12 | 5 |

[a] ADRs are defined as any Adverse Event that occurred within 24 hours after being infused with investigational product OR all Adverse Events assessed related or possibly related to investigational product OR Adverse Events for which the investigator's or sponsor's opinion of causality was missing or indeterminate.

[b] The ADVATE clinical program included 234 treated subjects from 5 completed studies in PTPs and 1 ongoing study in PUPs as of 27 March 2006.

[c] MedDRA version 8.1 was used.

**Table 2**
**Post-Marketing Experience**

| Organ System [MedDRA Primary SOC] | Preferred Term |
|---|---|
| Immune system disorders | Anaphylactic reaction[a]<br>Hypersensitivity[a] |
| Blood and lymphatic system disorders | Factor VIII inhibition |
| General disorders and administration site conditions | Injection site reaction<br>Chills<br>Fatigue/Malaise<br>Chest discomfort/pain<br>Less-than-expected therapeutic effect |

[a] These reactions have been manifested by dizziness, paresthesias, rash, flushing, face swelling, urticaria, and/or pruritus.

**References: 1.** Shapiro A, Gruppo R, Pabinger I et al. Integrated analysis of safety and efficacy of a plasma- and albumin-free recombinant factor VIII (rAHF-PFM) from six clinical studies in patients with hemophilia A. Expert Opin Biol Ther 2009 9:273-283. **2.** Tarantino MD, Collins PW, Hay PW et al. Clinical evaluation of an advanced category antihaemophilic factor prepared using a plasma/albumin-free method: pharmacokinetics, efficacy, and safety in previously treated patients with haemophilia A. Haemophilia 2004 10:428-437.

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## Hi! From our Executive Director

Dear Friends,

RMHBDA strives to provide diverse educational opportunities that add value to the lives of individuals affected with inherited bleeding disorders. There are few challenges greater than providing individuals and families with the knowledge, tools and resources they need to achieve independence; as it contributes to the well-being of their communities. All of our stakeholders — our members, our Board, our staff, and our volunteers — have benefited greatly from RMHBDA's good works. RMHBDA continues supporting families affected with inherited bleeding disorders in Montana and Wyoming by offering access to financial assistance, reasonable access to affordable healthcare, educational opportunities and resources, family and youth summer camp programs, and providing advocacy and awareness opportunities. I look forward to a bright and prosperous future for RMHBDA. If you have suggestions or concerns please feel free to contact me. This is your organization!

Thank you to our sponsors and donors for the continued support to enriching lives.

Sincerely,
Brad Benne