INFUSIONS

NEWSLETTER OF THE HEMOPHILIA FOUNDATION OF NORTHERN CALIFORNIA · WINTER 2015

Storming the capital

For more photos, see page 6.

PHOTO COURTESY OF SUZANE GOLDMAN

Pete Barbounis, Suzanne Goldman, Nancy Barbounis, Elizabeth Seaton, Dawn Pollard and Patrick Dunlap.

HFNC was well-represented at the annual meeting for the National Hemophilia Foundation in Washington, D.C. in September.

Overall, more than 3,000 people attended this year, and were welcomed by the theme "Nothing About Us Without Us." The setting could not have been more perfect for the theme, which weighed heavily on the topics of ensuring the hemophilia community has a voice when it comes to legislation that affects our community.

HFNC Board President Dawn Pollard led the charge in earning enough points in the "Bubble Buster Challenge," hosted by Biogen Idec Hemophilia, and with the help of the excited bubble busters pictured above, pushed HFNC into fourth place by the end of the event, earning $1,500 for the chapter.

There was plenty of education and networking to fill the weekend as well. Topics ranged from the Affordable Care Act to the challenges faced by community members working in the hemophilia industry.

The meeting adjourned until next August, when the national community will again come together in Dallas, Texas for the next meeting.

Big thanks for a big check

Rob and Margaret Storlee, owners of Rookies Sports Bar and Grill, in Benicia, came through big time in supporting Team Seaton/Mascoro for HFNC's annual Hemophilia Walk, raising $4,000 through a fundraiser that is expected to become an annual event.

They were thanked with a plaque that reads "Kids With Bleeding Disorders Love Rookies!"

Our thanks goes out to the Storlee for their past and future supprot of HFNC and our programs.

Next year's walk is planned for May 2, and it's never too early to start rallying your team, so get it on your calendars and start that fundraising now!

Baseball in the valley of the sun

Two families traveled from Northern California to Arizona for instruction in golf and baseball at the Gettin' in the Game Junior National Championship, hosted by CSL Behring.

Max Goldman represented Northern Calfornia well in the skills competition, taking home top prize for the 7-10 age group.

More than 100 kids participated in the event.

Contact Information

6400 Hollis Street, Suite 6
Emeryville, CA 94608

Office hours: Mon-Fri,
8:30 a.m. to 5 p.m.

www.hemofoundation.org

(510) 658-3324 phone
(510) 658-3384 fax

Donate your vehicle to support NHF and HFNC

Donate your car, boat, motorcycle, truck or other vehicle to NHF's Vehicle Donation Program. Visit NHF at www.hemophilia.org and click the "vehicle donation program" link, or call 1 (855) NHF-4-CAR. A representative will explain all of the details — including how to schedule free pick-up service that's convenient for you.

HFNC is going green!

Help HFNC reduce waste and cost by receiving *Infusions* via email. If you would like to make the switch, please email Patrick Dunlap at patrick.dunlap@hemofoundation.com.

Creating a Lifeline of Community and Support

Stories, sushi for brotherhood

The Blood Brotherhood group assembled at Moshi Moshi in San Francisco to hear stories from the life of Craig McLaughlin, a Berkeley resident living with hemophilia and author of the book "Lions and Tigers and AIDS, Oh, My!"

Craig is a professional storyteller who recently kicked off a one-man show in San Francisco and spreads his story in many different formats and settings. His expreiences have helped people from all walks of life face challenges in their lives with a new perpsective.

Blood Brotherhood continues to meet regularly under the direction of Dana Francis, social worker for adult hemophilia at UCSF.

For more information on the next meetings, contact HFNC.

D.A.O. poised to return

After a two-year hiatus, Disabled Adventure Outfitters is preparing to make a return to the whitewater of Northern California in 2015.

Following a restructuring of the boad of directors and a renewed push for fundraising, the organization is happy to announce that a teen camp is tentatively scheduled for the week of July 11-18 for youth ages 13 to 19.

Staff spots for adults may also be available, and the board is hoping to run a "vets camp" for adults next season as well.

D.A.O. has existed for more than 20 years with the goal of getting youth with bleeding disorders and other limitations outdoors, with a focus on whitewater rafting, rock climbing and camping. Participants will learn to pitch their own tents, cook their own food and spend the week on the river in Northern California.

Stay tuned to D.A.O.'s website (specialadventures.org) and Facebook page to get the latest news on how to apply for the program.

The Hemophilia Walk is NHF's largest event dedicated to finding better treatments and cures for bleeding and clotting disorders, and to preventing the complications of these disorders through awareness, education, advocacy and research. HFNC is proud to partner with NHF in sponsoring Hemophilia Walk in Berkeley this spring. Join hundreds of your friends and neighbors in raising funds and awareness about bleeding disorders.

WHEN: Saturday, May 2, 2015; registration at 9 a.m.
WHERE: Cesar Chavez Park, Berkeley

REGISTRATION IS NOW OPEN
Sign up your team today! Go www.hemophilia.org/walk and click CA Bay Area

Add these dates to your calendar for 2015

January

12	Board Meeting
16-18	Family Camp

February

9	Board Meeting
25-27	Washington Days

March

7	Crab Feed
9	Board Meeting
14	Family Information Day
26-28	HFA Symposium, St Louis

April

13	Board Meeting
17	World Hemophilia Day
26	Hemophilia Third Party Event - “Rookies”

May

2	NHF Walk
11	Board Meeting
11-13	HCC Future Leaders
13	Legislative Day
15-17	BLeaders Retreat

June

6	Board Retreat
14-20	Camp Hemotion

Other group meetings in 2015 being finalized: Blood Brotherhood, Female Factor, Dads in Action, Baseball Clinic, Asian Infusion.

July

8	Board Meeting
	Speeders for Bleeders
26-1	HCC Coastal Ride
31	Scholarship Applications Due

August

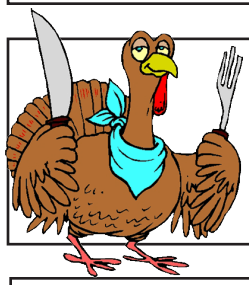
3	Board Meeting
9	HCC Advocacy Summit
9	Wine Tasting Event
10	Golf Tournament
13-15	NHF Annual Meeting
TBD	Taylor Family Day in the Park

September

14	Board Meeting

October

12	Board Meeting
17	Fresno Wine Tour
TBD	Hispanic Heritage Celebration



November

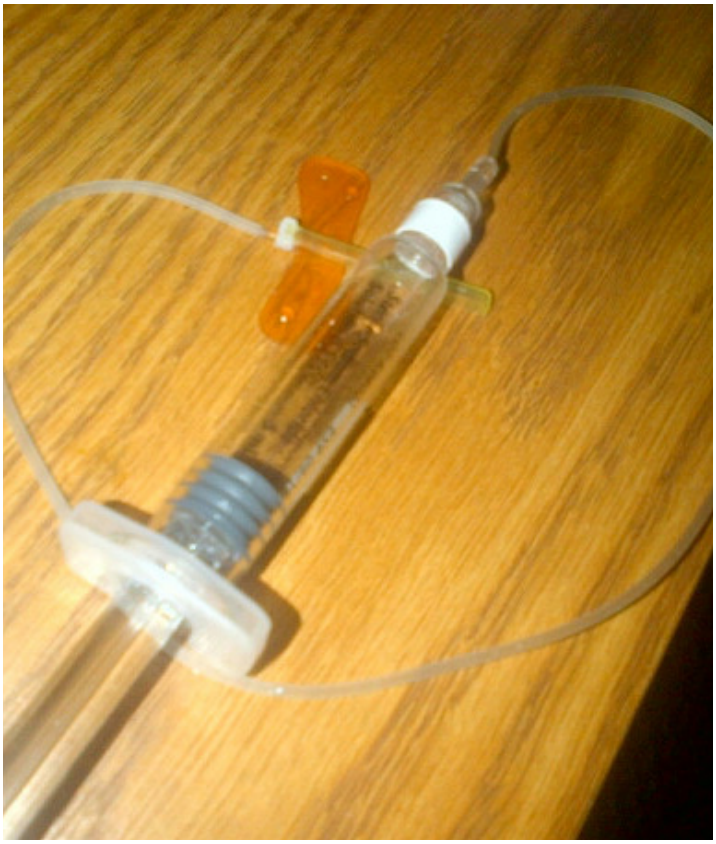
9	Board Meeting

December

6	Holiday Party Oakland
12	Holiday Party Madera
13	Holiday Party Modesto

FDA Approves RIXUBIS for Treatment of Children

Baxter International Inc. announced that the United States Food and Drug Administration (FDA) has approved RIXUBIS [Coagulation Factor IX (Recombinant)] for routine prophylactic treatment, control and prevention of bleeding episodes, and perioperative management in children with hemophilia B. RIXUBIS was the first recombinant factor IX (rFIX) approved for routine prophylaxis and control of bleeding episodes in the U.S. for adults living with this chronic condition.



"In addition to the positive reception we've received from adult RIXUBIS patients, the approval for pediatric patients offers a valuable new option, particularly as our clinical data demonstrated a significant reduction in bleeding episodes for patients who were treated prophylactically, an important factor for this young patient population," said John Orloff, M.D., vice president of global research and development at Baxter BioScience.

The approval is based on the results of a clinical trial investigating the efficacy and safety of RIXUBIS among 23 previously-treated male patients less than 12 years of age with severe or moderately severe hemophilia B. The patients were treated with a twice-weekly RIXUBIS prophylaxis regimen (mean dose 56 IU/kg) for a mean treatment duration of six months and a mean of 54 exposure days (EDs). The median annualized bleeding rate (ABR) was 2.0 (0.0 for spontaneous bleeds and joint bleeds). Nine patients in the study (39.1%) experienced no bleeds and 23 bleeding episodes (88.5%) were treated with 1-2 infusions. There were no reports of inhibitor development, no severe allergic reactions, and no thrombotic or treatment-related adverse events among the study participants. Common adverse reactions observed in >1% of subjects in clinical studies were dysgeusia, pain in extremity, and positive test for furin antibody. These data were presented during the 55th Annual Meeting of the American Society of Hematology (ASH) in New Orleans, LA.

Baxter's application for marketing approval for RIXUBIS for adults and pediatric patients is currently under review in the European Union,

Continued on page 17

Medscape Education Activity Focuses on Clinical Management Challenges

"Current Challenges in Managing Hemophilia," the latest online educational activity from Medscape, became available on Tuesday, May 20, 2014. It is intended for hematologists, pediatricians, nurses, and other healthcare professionals who manage patients with hemophilia.

The goal of the program is to increase the knowledge, skills and competence of clinicians, to facilitate optimal, individualized management of hemophilia.

The activity features experts in the management of hemophilia who provide insights based in their clinical expertise and experience.

This latest activity is part of Clinical Advances in Hemophilia: Management for Life, a series of educational activities provided by leading bleeding disorders clinicians.

The series is presented through a strategic collaboration by the Perelman School of Medicine at the University of Pennsylvania, the National Hemophilia Foundation and Medscape Education Hematology.

After completing these activities, available for one year from their upload date, those eligible may receive continuing education (CE) or continuing medical education (CME) credits:

"Current Challenges in Managing Hemophilia" CME/CE

Patrick F. Fogarty, MD; Keith Gomez, PhD, MRCP, FRCPath; Andreas Tiede, MD, PhD

CME/CE Released: 05/20/2014; Valid for credit through 05/20/2015

To access this and other available educational opportunities go to www.medscape.com. Once registered you may access Clinical Advances in Hemophilia: Management for Life.

Clockwise from upper left: Dawn Pollard, Shelley Jajeh, Suzanne Goldman and Nancy Barbounis enjoy lunch; Nancy and Pete Barbounis show off their keen fashion sense; Patrick Dunlap pops some digital bubbles to raise money for HFNC; Marilyn August, Nancy and Pete Barbounis, Dawn Pollard and Suzanne Goldman smile for the camera; Patrick Dunalp poses with Robert Seaton and his daughter, Elizabeth Seaton.

FDA approves first combination pill for treatment of hepatitis C

The U.S. Food and Drug Administration today approved Harvoni (ledipasvir and sofosbuvir) to treat chronic hepatitis C virus (HCV) genotype 1 infection.

Harvoni is the first combination pill approved to treat chronic HCV genotype 1 infection. It is also the first approved regimen that does not require administration with interferon or ribavirin, two FDA-approved drugs also used to treat HCV infection.

Both drugs in Harvoni interfere with the enzymes needed by HCV to multiply. Sofosbuvir is a previously approved HCV drug marketed under the brand name Sovaldi. Harvoni also contains a new drug called ledipasvir.

"With the development and approval of new treatments for hepatitis C virus, we are changing the treatment paradigm for Americans living with the disease," said Edward Cox, M.D., M.P.H., director of the Office of Antimicrobial Products in the FDA's Center for Drug Evaluation and Research. "Until last year, the only available treatments for hepatitis C virus required administration with interferon and ribavirin. Now, patients and health care professionals have multiple treatment options, including a combination pill to help simplify treatment regimens."

Harvoni is the third drug approved by the FDA in the past year to treat chronic HCV infection. The FDA approved Olysio (simeprevir) in November 2013 and Sovaldi in December 2013.

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people infected with HCV have no symptoms of the disease until liver damage becomes apparent, which may take decades.

Some people with chronic HCV infection develop scarring and poor liver function (cirrhosis) over many years, which can lead to complications such as bleeding, jaundice (yellowish eyes or skin), fluid accumulation in the abdomen, infections and liver cancer. According to the Centers for Disease Control and Prevention, about 3.2 million Americans are infected with HCV, and without proper treatment, 15-30 percent of these people will go on to develop cirrhosis.

Harvoni's efficacy was evaluated in three clinical trials enrolling 1,518 participants who had not previously received treatment for their infection (treatment-naive) or had not responded to previous treatment (treatment-experienced), including participants with cirrhosis. Participants were randomly assigned to receive Harvoni with or without ribavirin. The trials were designed to measure whether the hepatitis C virus was no longer detected in the blood at least 12 weeks after finishing treatment (sustained virologic response, or SVR), indicating that a participant's HCV infection has been cured.

In the first trial, comprised of treatment-naive participants, 94 percent of those who received Harvoni for eight weeks and 96 percent of those who received Harvoni for 12 weeks achieved SVR. The second trial showed 99 percent of such participants with and without cirrhosis achieved SVR after 12 weeks. And in the third trial, which examined Harvoni's efficacy in treatment-experienced participants with and without cirrhosis, 94 percent of those who received Harvoni for 12 weeks and 99 percent of those who received Harvoni for 24 weeks achieved SVR. In all trials, ribavirin did not increase response rates in the participants.

The most common side effects reported in clinical trial participants were fatigue and headache.

Harvoni is the seventh new drug with breakthrough therapy designation to receive FDA approval. The FDA can designate a drug as a breakthrough therapy at the request of the sponsor if preliminary clinical evidence indicates the drug may demonstrate a substantial improvement over available therapies for patients with serious or life-threatening diseases. Harvoni was reviewed under the FDA's priority review program, which provides for an expedited review of drugs that treat serious conditions and, if approved, would provide significant improvement in safety or effectiveness.

Harvoni and Sovaldi are marketed by Gilead, based in Foster City, California. Olysio is marketed by Janssen Pharmaceutical based in Raritan, New Jersey.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

Emerging Public Health Needs of Persons with Blood Disorders

By Christopher S. Parker, PhD, James Tsai, MD, MPH, Azfar-e-Alam Siddiqi, MD, PhD, Hani K. Atrash, MD, MPH, Lisa C. Richardson, MD, MPH

In its decades-long history, the Division of Blood Disorders (DBD) at CDC has evolved from a patient-focused, services-supporting entity at inception, to one of the world leaders in the practice of public health to improve the lives of people at risk for or affected by nonmalignant blood disorders. The DBD's earliest public health activities consisted of working with care providers in a network of hemophilia treatment centers to provide AIDS risk reduction services to people with hemophilia.

Because this infectious disease threat has been reduced over time as a result of the development of safer treatment products, the DBD—under the auspices of congressional appropriations guidance— has expanded its core activities to encompass blood disorders other than hemophilia, including hemoglobinopathies such as thalassemia and sickle cell disease, and Diamond Blackfan anemia. Simultaneously, in transitioning to a greater public health role, the DBD has expanded its network of partners to new consumer and professional organizations, as well as state and other federal health agencies.

The DBD has also developed and maintains many surveillance and registry activities beyond the Universal Data Collection system aimed at providing a better understanding of the health status, health needs, and health-related quality of life of people with nonmalignant blood disorders. The DBD has integrated applicable components of the Essential Services of Public Health successfully to promote and advance the agenda of blood disorders in public health.

A Public Health Approach to the Prevention of Inhibitors in Hemophilia

By J. Michael Soucie, PhD, Connie H. Miller, PhD, Fiona M. Kelly, MPH, Meredith Oakley, DVM, MPH, Deborah L. Brown, MD, Phillip Kucab, MD

The development of an antibody in people with hemophilia to products used in the treatment and prevention of bleeding, also referred to as an inhibitor, is the most serious complication of hemophilia care today.

The CDC, together with healthcare providers, consumer organizations, hemophilia organizations, and federal partners, has developed a public health agenda to prevent the development of inhibitors.

This paper describes a public health approach that combines a national surveillance program with epidemiologic, laboratory, and prevention research to address knowledge gaps in rates and risk factors for inhibitor development, and in knowledge and behaviors of patients and providers, in addition to screening and treatment practices.

Public Health Surveillance of Nonmalignant Blood Disorders

By Michele G. Beckman, MPH, Mary M. Hulihan, MPH, Vanessa R. Byams, MPH, Meredith A. Oakley, DVM, MPH, Nimia Reyes, MD, Sean Trimble, MPH, Althea M. Grant, PhD, MPH

Nonmalignant blood disorders currently affect millions of Americans, and their prevalence is expected to grow over the next several decades. This is owing to improvements in treatment leading to increased life expectancy of people with hereditary conditions, like sickle cell disease and hemophilia, but also the rising occurrence of risk factors for venous thromboembolism.

The lack of adequate surveillance systems to monitor these conditions and their associated health indicators is a significant barrier to successfully assess, inform, and measure prevention efforts and progress toward national health goals. CDC is strengthening surveillance activities for blood disorders by improving and developing new methods that are tailored to best capture and monitor the epidemiologic

characteristics unique to each disorder. These activities will provide a robust evidence base for public health action to improve the health of patients affected by or at risk for these disorders.

Blood Disorders and Public Health

By Lisa C. Richardson, MD, MPH, Christopher S. Parker, PhD, MPH, James Tsai, MD, MPH

Millions of people in the U.S. are affected by blood disorders.1 The accumulating epidemiologic evidence for non-malignant blood disorders continues to strengthen its consideration as a national public health priority. Although there is enormous potential for public health practice to reduce the disease burden and associated healthcare costs, the fiscal resources with which to do so are decreasing and may continue in the near future. Thus, the Division of Blood Disorders at the Centers for Disease Control and Prevention has embraced a new currency of developing and implementing a comprehensive set of public health approaches to effectively promote and improve the health of people with blood disorders.

Providing Young Women with Credible Health Information

By Patricia A. Rhynders, PhD, MPH, MCHES, Cynthia A. Sayers, BA, Rodney J. Presley, PhD, JoAnn M. Thierry, PhD

Approximately 1% of U.S. women may have an undiagnosed bleeding disorder, which can diminish quality of life and lead to life-threatening complications during menstruation, childbirth, and surgery. To understand young women's knowledge, attitudes, and perceptions about bleeding disorders and determine the preferred messaging strategy for presenting information a web-assisted personal interview of 1,243 women aged 18–25 years was conducted. The study showed that participants knew that a bleeding disorder is a condition in which bleeding takes a long time to stop (77%) or blood does not clot (66%).

Also, 57% incorrectly thought that a bleeding disorder is characterized by thin blood; and, many were unsure if bleeding disorders involve blood types, not getting a period, or mother and fetus having a different blood type. Women at risk for a bleeding disorder were significantly more likely to report that menstruation interfered with daily activities (36% vs 9%); physical or sports activities (46% vs 21%); social activities (29% vs 7%); and school or work activities (20% vs 9%) than women not at risk. Gain-framed messages were significantly more likely to influence women's decisions to seek medical care than parallel loss-framed messages.

Findings suggest that the most influential messages focus on knowing effective treatment is available; preventing pregnancy complications; and maintaining typical daily activities during menstrual periods. Lack of information about bleeding disorders is a serious public health concern. Credible information and preferred health communication messaging focused on gain-framed statements might encourage symptomatic young women to seek diagnosis and treatment. These findings and corresponding recommendations align with Healthy People 2020 and with the CDC's goal of working to promote the health, safety, and quality of life of women at every life stage.

Researchers May Have Found Trick to Slow HIV

The region of the DNA to which the HIV virus binds itself is what determines how quickly the disease progresses, says a new study.

By retargeting the integration site to a 'safer' part of the host DNA, new therapies for Aids can be developed.

The human immunodeficiency virus (HIV) binds and invades human immune cells where it reprogrammes the human DNA to produce new HIV. The HIV protein integrase plays a crucial role by identifying a segment of the host DNA and orchestrating the manipulation of the DNA.

While the viral DNA can be inserted at many places on the strand, how it picks certain sections has been unknown.

Proteins are long chains of amino acids. In the viral integrase, the researchers found two amino acids that determine the integration site.

KU Leuven researcher Jonas Demeulemeester, first author of the study, explains: "HIV integrase is made up of a chain of more than 200 amino acids folded into a structure. By modelling this structure, we found two positions in the protein that make direct contact with the DNA of the host. These two amino acids determine the integration site. This is not only the case for HIV but also for related animal-borne viruses."

By replacing these amino acids by those of other animal-borne viruses, they saw that the viral DNA integrated into the host DNA at different locations. The study also showed that the viral protein in HIV can vary with different amino acids appearing in the positions.

Most important, the work showed rapid progression of Aids when they changed the integration site.

The study by KU Leuven's Laboratory for Molecular Virology and Gene Therapy and University of KwaZulu-Natal, Durban, South Africa was published online in the journal Cell Host & Microbe.

The fast mutating HIV has eluded a cure despite many claims in the recent past. The latest is the case of two men infected years ago who never developed Aids and have ndetectable levels of HIV.

The virus was inactivated because its genetic code had been altered, said the researchers linking this to increased activity of a common enzyme Apobec. However, experts have questioned the accuracy and quality of the research, reports Newsweek.

WANT TO KNOW MORE ABOUT YOUR FACTOR OPTIONS?

When it comes to your factor therapy, you have choices. And at Biogen Idec, we recognize the importance of researching and delivering additional factors to the hemophilia community. See if now might be the right time for you to make a change—learn more about our therapy options as well as our range of financial, educational, and community support programs.

TO LEARN MORE ABOUT THESE OPTIONS, CONTACT YOUR CoRe MANAGER:
Marilyn August | **Phone:** 925.864.0547 | **E-mail: Marilyn.August@biogenidec.com**

biogen idec.

MORE THAN JUST ANOTHER LINE ON YOUR RESUME

Making a change in the world begins by making a change in your community! Apply to be an intern through the Bayer Hemophilia Leadership Development Program and begin to learn how to be the change YOU want to see in the world.

Students enrolled full-time in college who are touched by hemophilia can apply now for the opportunity to:

- Engage in leadership training and hands-on business projects
- Learn how to support the hemophilia community as a potential future leader

Apply now for a six-week paid internship at Bayer HealthCare's U.S. headquarters in New Jersey.

In addition to working directly with leaders at Bayer, selected interns will:

- Collaborate with local hemophilia organizations and learn about efforts to support the hemophilia community and partnerships with business professionals
- Meet with healthcare public policy professionals to experience first-hand how effective advocacy relations impacts legislative decisions
- Be responsible for developing a project that will be presented to Bayer Senior Management

Start shaping your future and your community!

Apply today for the Bayer Hemophilia Leadership Development Program.

APPLICATIONS ARE DUE NO LATER THAN **Friday, March 13, 2015 at 11:59 p.m. ET**
To learn more and complete an application, visit www.HemophiliaInternship.com

BAYER HEMOPHILIA LEADERSHIP DEVELOPMENT PROGRAM

Explore Bayer HealthCare's additional leadership opportunities, Step Up Reach Out and AFFIRM, at **www.hemophilialead.net.**

PASSION + ADVOCACY + REAL WORLD EXPERIENCE

Bayer HealthCare

Baxter

UNLOCKING YOUR SELF-POTENTIAL

ADVATE Prophylaxis May Help You Prevent or Reduce Bleeds[1]

Significant reduction in median annual bleed rate (ABR) with prophylactic treatment compared with on-demand treatment[1]

In a clinical study, after switching from 6 months of on-demand treatment to 12 months of prophylaxis with ADVATE in 53 previously treated patients (PTPs) with severe or moderately severe hemophilia A. The clinical study evaluated treatment efficacy (the ability to control and reduce bleeds) of 2 prophylaxis regimens – Every-Second-Day (standard) prophylaxis dosed at 20 to 40 IU/kg every 48 hours and Every-Third-Day (pharmacokinetic-driven) prophylaxis dosed at 20 to 80 IU/kg every 72 hours, targeted to maintain factor VIII trough levels ≥1%.

- 0 bleeds experienced by 42% of patients during 1 year on prophylaxis
- 98% reduction in median ABR from 44 to 1 when switched from on-demand to prophylaxis
- 97% reduction in median annual joint bleed rate from 38.7 to 1 after switching from on-demand to prophylaxis
- No subject developed factor VIII inhibitors or withdrew due to an adverse event (AE)[2]

INDICATIONS

ADVATE 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 adults and children (0-16 years) with hemophilia A. Your healthcare provider may give you ADVATE when you have surgery. ADVATE can reduce the number of bleeding episodes in adults and children (0-16 years) when used regularly (prophylaxis).

ADVATE is not used to treat von Willebrand Disease.

DETAILED IMPORTANT RISK INFORMATION

You should not use ADVATE if you:

- Are allergic to mice or hamsters.
- Are allergic to any ingredients in ADVATE.

Tell your healthcare provider if you are pregnant or breastfeeding because ADVATE may not be right for you.

You should tell your healthcare provider if you:

- Have or have had any medical problems.
- Take any medicines, including prescription and non-prescription medicines, such as over-the-counter medicines, supplements or herbal remedies.
- Have any allergies, including allergies to mice or hamsters.
- Have been told that you have inhibitors to factor VIII (because ADVATE may not work for you).

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.

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.

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

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

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.

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

Ask your healthcare provider if prophylaxis with ADVATE is right for you.

ADVATE
[Antihemophilic Factor (Recombinant)]
There's more to life.

www.advate.com | 888.4.ADVATE

References: 1. ADVATE Prescribing Information. Westlake Village, CA: Baxter Healthcare Corporation; April 2014. **2.** 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.

ADVATE [Antihemophilic Factor (Recombinant)]
Lyophilized Powder for Reconstitution for Intravenous Injection
Brief Summary of Prescribing Information: Please see package insert for full Prescribing Information.

INDICATIONS AND USAGE

ADVATE [Antihemophilic Factor (Recombinant)] is a recombinant antihemophilic factor indicated for use in children and adults with hemophilia A (congenital factor VIII deficiency or classic hemophilia) for:

- Control and prevention of bleeding episodes.
- Perioperative management.
- Routine prophylaxis to prevent or reduce the frequency of bleeding episodes.

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

CONTRAINDICATIONS

ADVATE is contraindicated in patients who have life-threatening hypersensitivity reactions, including anaphylaxis, to mouse or hamster protein or other constituents of the product (mannitol, trehalose, sodium chloride, histidine, Tris, calcium chloride, polysorbate 80, and/or glutathione).

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Allergic-type hypersensitivity reactions, including anaphylaxis, have been reported with ADVATE. Symptoms include dizziness, paresthesia, rash, flushing, facial swelling, urticaria, dyspnea, and pruritus.

ADVATE contains trace amounts of mouse immunoglobulin G (MuIgG) ≤0.1 ng/IU ADVATE, and hamster proteins ≤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

Neutralizing antibodies (inhibitors) have been reported following administration of ADVATE predominantly in previously untreated patients (PUPs) and previously minimally treated patients (MTPs). Monitor all patients for the development of factor VIII inhibitors by appropriate clinical observation and laboratory testing. 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

- 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*]
- 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 reactions seen with ADVATE are hypersensitivity reactions and the development of high-titer inhibitors necessitating alternative treatments to factor VIII.

The most common adverse reactions 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 clinical trials in previously treated patients (PTPs) and one ongoing trial 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 (range: 1 to 598).[3]

The summary of adverse reactions with a frequency ≥5% (defined as adverse events occurring within 24 hours of infusion or any adverse event causally related occurring within the trial period) is shown in Table 3.

No subject was withdrawn from a clinical trial due to an adverse reaction. There were no deaths in any of the clinical trials.

Table 3
Summary of Adverse Reactions[a] with a Frequency ≥5% (N = 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] Adverse reactions are defined as all adverse events that occurred (a) within 24 hours after being infused with investigational product, or (b) all adverse events assessed related or possibly related to investigational product, or (c) 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 trial in PUPs as of 27 March 2006.

[c] MedDRA version 8.1 was used.

Immunogenicity

The development of factor VIII inhibitors with the use of ADVATE was evaluated in clinical trials 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 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).[3,4] No factor VIII inhibitors were detected in the 53 treated pediatric PTPs.

In clinical trials 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.[3] Four subjects 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 subjects, 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.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to ADVATE with the incidence of antibodies to other products may be misleading.

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 4 represents the most frequently reported post-marketing adverse reactions as MedDRA Preferred Terms.

Table 4
Post-Marketing Experience

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

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

Baxter Healthcare Corporation, Westlake Village, CA 91362 USA
U.S. License No. 140 Issued 04/2014
USBS/34/14-0104

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Prophylaxis Helps Man Lower His Annual Bleed Rate

Luis Estrada had a rough start in life. As a toddler in Costa Rica, Luis fell and became paralyzed from his chest down to his feet. A few months earlier, his father had died in a car accident, forcing his mother to work full-time away from home to support Luis and his two sisters.

"My friends would get me to and from school, and play with me in the sugar cane fields," Luis recalls. "I had support from good people."

Doctors diagnosed Luis with severe hemophilia A shortly after his birth. In the late 1950s and early 1960s in Costa Rica, blood transfusions were his only treatment.

His family inspired him to be responsible and self-reliant. "A cousin would tell me that I wasn't disabled, that I could help to do the chores around the house, so I learned to do things for myself, like cooking, cleaning, and sewing."

Despite his challenges, Luis says he had a great childhood. "When I was about seven or eight, I'd play goalie during easy soccer games with my friends. I was pretty good in my wheelchair," he remembers fondly.

Luis and his family moved to San Francisco when he was a teenager. Like most teenagers, Luis wanted to be as active and mobile as possible.

"When I had bleeds in my left shoulder and elbow, I'd start using my right arm so I could keep moving," explains Luis. "Eventually my right shoulder and elbow would bleed, so I'd switch back to using my left arm. Then those joints would bleed again. It got so bad that I was going to the hospital just about every week. Sometimes I'd be admitted for a few days, other times for a week or two."

Luis has been married to his wife, Laura, since 2000. She will never forget Luis' frequent hospital stays. "It was horrible to see him in pain," Laura recalls. "I was frustrated and angry because I couldn't help him, but I had to suppress my feelings. It was exhausting."

"Laura was always supporting me, forcing me to go to the hospital even when I didn't want to," Luis says. "I knew it was very hard for her to see me so uncomfortable."

"Before I started infusing prophylactically, my annual bleed rate was over 50. Now my ABR is down to five or six..."

— Luis Estrada

Luis switches to prophylaxis

Luis' doctor eventually prescribed a prophylaxis regimen with ADVATE [Antihemophilic Factor (Recombinant)], a medicine used to replace clotting factor VIII that is missing in people with hemophilia A. It can reduce the number of bleeding episodes in adults and children (0-16 years) when used regularly (prophylaxis). Luis infuses every other day.

You can hear the gratitude in Luis' voice. "Before I started infusing prophylactically, my annual bleed rate was over 50. Now my ABR is down to five or six."

"Now I have more time for myself. I go out with friends for coffee or lunch. I'm doing yoga and studying for my degree in art and sociology."

Luis and Laura love to travel together. They have visited cities across the U.S., and have made several trips to Costa Rica to visit their families. Luis has also returned to a favorite activity of his youth. "I love kicking around a soccer ball with my four-year-old nephew. He likes when I play goalie, just as I did when I was only a few years older than he is now."

According to Laura, "They love each other, they're good for each other and they definitely help each other."

Selected Important Risk Information

You should not use ADVATE [Antihemophilic Factor (Recombinant)] if you:

- Are allergic to mice or hamsters.
- Are allergic to any ingredients in ADVATE.

Side effects that have been reported with ADVATE include cough, headache, joint swelling/aching, sore throat, fever, itching, unusual taste, dizziness, hematoma, abdominal pain, hot flashes, swelling of legs, diarrhea, chills, runny nose/congestion, nausea/vomiting, sweating, and rash. Tell your healthcare provider about any side effects that bother you or do not go away.

Please see next page for ADVATE Detailed Important Risk Information.

Learn more about Luis and other real people's inspiring stories by visiting Baxter's www.yourtrueid.com.

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Pfizer

Continued from page 5

with a regulatory decision expected later this year. The treatment also recently gained regulatory approval in Australia.

RIXUBIS [Coagulation Factor IX (Recombinant)] is an antihemophilic factor indicated in adults and children with hemophilia B for control and prevention of bleeding episodes, perioperative management, and routine prophylaxis. RIXUBIS is not indicated for induction of immune tolerance in patients with hemophilia B.

RIXUBIS was the first rFIX approved by the FDA for both routine prophylaxis and control of bleeding episodes in adults.

Hemophilia Foundation
of Northern California
6400 Hollis St · Suite 6
Emeryville, CA 94608

The Hemophilia Foundation of Northern California

Creating a Lifeline of Community and Support

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The Infusions Newsletter is underwritten yearly by generous grants from Baxter and Bayer.

Infusions staff

Ben Martin
EDITING AND LAYOUT

Suzanne Goldman
Dawn Pollard
CONTRIBUTING PHOTOGRAPHER(S)

Ben Martin
CONTRIBUTING WRITER

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