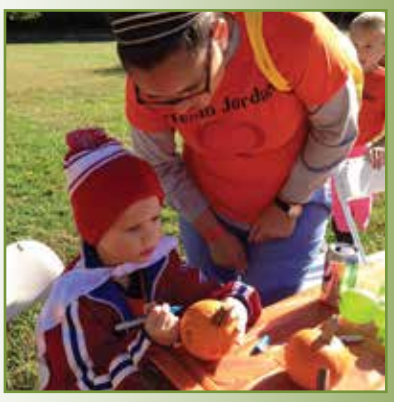
Winter 2015

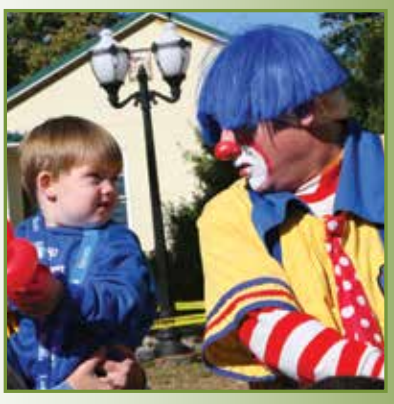
KHF Hemosphere

Great day for a Walk2 cure hemophilia in the park!

Nearly two hundred walkers participated in KHF's second annual Hemophilia Walk in October. It was a pleasant day for this outdoor activity at Wetherby Park in Middletown. Everyone from the bleeding disorders community in our state and beyond and the community at large is invited to support this yearly event for a very worthy cause.



In addition to raising funds that allow KHF to make a positive difference in the lives of men, women, and children with hemophilia and similar bleeding disorders, this event fosters a sense of community and empowerment among the families that gather to walk and fundraise so we can help them and others with educational and advocacy programs and supportive services that we provide to nearly one thousand families in our area.



The atmosphere at the event was one of joy and re-assurance. It was shared and felt by all. Teams consisting of family and friends showcasing colorful t-shirts and individual walkers, some with kiddos in strollers, filed through the park accompanied by lively music. After the Walk, participants enjoyed hot dogs and popcorn, while the children had the opportunity to play in the bouncy house, visit the clowns, and paint pumpkins.

A sea of sunny, yellow Walk shirts and yellow Walk tote bags could be seen from every vantage point, reinforcing the heart-warming and uplifting spirit that emanated from the crowd of walkers. The event culminated in the awarding of prizes for most monies raised by teams and individuals as determined by totals on the day of the event. We congratulate and thank all teams and walkers who participated and fundraised for a cause near and dear to all involved.

For the Walk Team winners and more Walk news, please see page 6.

Health News

FDA Approves Baxalta's Longer Lasting Therapy for Hemophilia A

The US Food and Drug Administration (FDA) recently approved Baxalta's ADYNOVATE, a new longer-lasting recombinant factor VIII (rFVII) product. The new therapy is indicated for the on-demand treatment of bleeding episodes, and for routine prophylaxis in adult and adolescent patients (12 years and older) with hemophilia A. The production of ADYNOVATE includes the use of polyethylene glycol (PEGylated) molecules that keep the rFVIII circulating in the blood for longer periods, potentially leading to less frequent infusions.

Final FDA approval was based on the results of a phase 3 clinical trial that measured the safety and efficacy of ADYNOVATE in 137 adults and adolescents 12 years of age and older. The subjects came from 20 countries, including the US, Australia, Japan and Spain.

Investigators found that ADYNOVATE demonstrated efficacy in treating hemophilia patients using routine prophylaxis and for on-demand bleeding episodes. The results showed that previously treated patients who received the therapy prophylactically twice weekly experienced 95% fewer annual bleeds compared to those who were treated on-demand. 96% of the bleeding episodes that occurred during the study were controlled with one or two infusions. Lastly, no patients developed inhibitors to the treatment and no safety concerns arose during the study. Adverse effects were only seen in 1% of the subjects, the most common of which were headache and nausea.

"The approval of ADYNOVATE provides an important therapeutic option for use in the care of patients with hemophilia A and reduces the frequency of factor VIII infusions needed to avoid bleeding," said Karen Midthun, MD, director of the FDA's Center for Biologics Evaluation and Research.

Source: *FDA news release and Baxalta press release, both dated November 13, 2015*

FDA Approves Coagadex®, First Factor X Concentrate

The US Food and Drug Administration (FDA) approved Coagadex®, Coagulation Factor X (Human), for hereditary factor X (FX) deficiency. Until today's orphan drug approval, no specific coagulation factor replacement therapy was available for patients. In healthy individuals, the FX protein activates enzymes to help with normal blood clotting in the body. FX deficiency is an inherited disorder affecting men and women equally in which the blood does not clot as it should. Patients with the disorder are usually treated with fresh-frozen plasma or plasma-derived prothrombin complex concentrates (plasma products containing a combination of vitamin K-dependent proteins) to stop or prevent bleeding. The availability of a purified FX concentrate increases treatment options for patients with this rare bleeding disorder.

"The approval of Coagadex is a significant advancement for patients who suffer from this rare but serious disease," said Karen Midthun, MD, director of the FDA's Center for Biologics Evaluation and Research.

Coagadex, which is derived from human plasma, is indicated for individuals aged 12 and older with hereditary FX deficiency for on-demand treatment and control of bleeding episodes, and for perioperative (period extending from the time of hospitalization for surgery to the time of discharge) management of bleeding in patients with mild hereditary FX deficiency.

The safety and efficacy of Coagadex were evaluated in a multi-center, nonrandomized study involving 16 participants (208 bleeding episodes) for treatment of spontaneous, traumatic and heavy menstrual (menorrhagic) bleeding episodes. Coagadex was demonstrated to be effective in controlling bleeding episodes in participants with moderate to severe hereditary FX deficiency. It was also evaluated in five participants with mild to severe FX deficiency who were undergoing surgery. The five individuals received Coagadex for perioperative management of seven surgical procedures. Coagadex was demonstrated to be effective in controlling blood loss during and after surgery in participants with mild deficiency. No individuals with moderate or severe FX deficiency received Coagadex for perioperative management of major surgery, and no safety concerns were identified in either study.

The FDA granted Coagadex orphan product designation for these uses. Orphan product designation is given to drugs intended to treat rare diseases in order to promote their development. Coagadex was also granted fast track designation and priority review.

Coagadex is manufactured by Bio Products Laboratory Limited in Elstree, Hertfordshire, United Kingdom.

Source: NHF, October 21, 2015

Event News

Gettin' in the Game

Two youngsters from Louisville won the drawing for attending CSL Behring's Gettin' in the Game Junior Championships. Daphne Powell and Peyton Oliver travelled to Phoenix, AZ to represent KHF. Daphne participated in the golfing event and Peyton in the baseball event. They enjoyed the instruction and activities provided as well as meeting boys and girls from all over the United States. This program, developed and sponsored by CSL Behring, emphasizes the importance of physical activity for youngsters with bleeding disorders in order to achieve and maintain overall wellness and good health and strives to empower participants to engage in recommended sports.

Swimming at the YMCA

A dozen children and their parents enjoyed the swimming demonstration and educational information provided by Tim Grams, a Gettin' in the Games Athlete who has hemophilia A, at the YMCA pool in Louisville followed by open swim time and pool play. Tim is a former collegiate swimmer and record holder. Jimmy John's sandwiches provided needed energy for frolicking in the water. Swimming is a low-impact sport that is very beneficial for youngsters with bleeding disorders. Swimming promotes joint mobility and strengthening of muscles and is so much fun! We thank CSL Behring for sponsoring this important program for our youngsters.

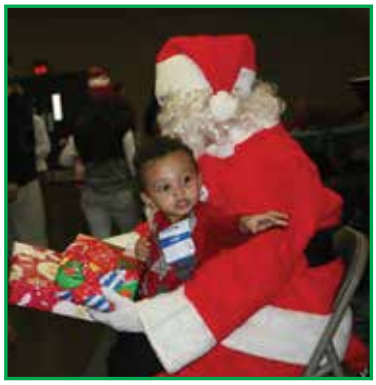
VWD Retreat for Women and Girls

The VWD Retreat for Women and Girls took place in beautiful Berea, KY. Participants enjoyed accommodations and meals at the historic Boone Tavern Hotel in this quaint college town that brims with galleries and workshops featuring fine art and Appalachian crafts. A getting acquainted dinner on Friday night was followed by zumba and movies. On Saturday morning, several speakers including Patricia Ashby, ARNP, and Diane Burnett, PNP, from the Louisville Adult and Pediatric HTC's (Hemophilia Treatment Centers) discussed topics associated with von Willebrand disease and addressed questions and concerns expressed by the participants.

After lunch, the retreat concluded with a jewelry making workshop provided by Bob and Scott Mattingly. We thank CSL Behring for sponsoring this successful program for women and girls in Kentucky's bleeding disorders community.

Event News

Holiday Festivities

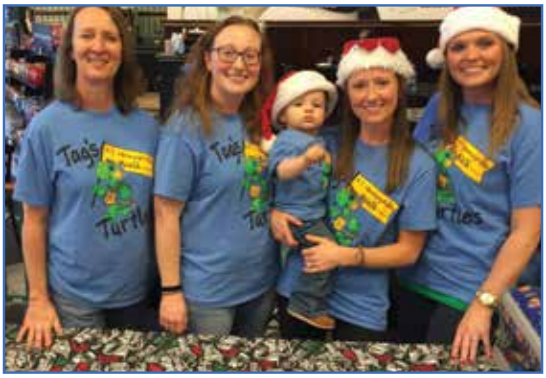


Close to two hundred attendees enjoyed KHF's holiday festivities at the Highland Legion Post in Louisville. In addition to sampling the delectable food items provided by Chef John Taylor, enjoying the musical entertainment by our very own David Pitt, guests were mixing and mingling with old and new friends. They also visited with exhibitors and perused an attractive selection of silent auction items. A record number of fourteen baked items were entered in the annual bake contest, which was won by Glenn Webb of Louisville with his Banana Pudding Cake. Runner up was Ireland Masticola of Louisville who entered her Chess Bars and in third place was Karen Lucky of Cynthiana, who entered her Pecan Pie. Santa brought presents for all youngsters in attendance. Adults received gifts as well via the drawing of many door prizes. Judging by all the smiles, it was a wonderfully uplifting event. Many thanks to all our volunteers who helped organize this event and our donors and sponsors who were Accredo, Baxalta, Bayer Healthcare, Biogen, CSL Behring, CVS Caremark, Emergent, Factor 4 Life, Grifols, Susan & Jack Leffew, and Matrix Health.

Poinsettia Fundraiser

The annual poinsettia sale is our longest running fundraiser. We appreciate all of our volunteers who faithfully promote the sale amidst much competition from other non-profit entities and retail stores and continue to generate orders for us! We sold a total of 2,765 plants this holiday season. Our primary volunteers are Janet Goff and Sharon McMahan from Owensboro, Pat Cooper from the Kentucky Blood Center in Lexington, Jenifer Schultz from New Albany, IN, Tina Pelly from Campbellsville, Sadalia Sturgill from Lebanon Junction, Marion Forcht from Corbin, and Deborah Hitt from Shelbyville. Louisville volunteers were Eric Marcum, Diane Burnett, Jim Lueken, Nita Wayne Zehnder, and the family of Betty Meadors Mattingly. A special acknowledgement goes to Janet Goff and her daughter Sharon for their achievement. They ordered 376 poinsettias or 13.6 percent of the overall total for churches and individuals in the Owensboro area. Many thanks to all who participated in and supported this fundraiser to help us fund our programs and services!

Wrapping Gifts at Barnes & Noble Fundraiser



Amanda Houchens and three other members of Walk Team "Tag's Turtles" carried forward the spirit of the Kentucky Hemophilia Walk by volunteering their time to wrap gifts at Barnes & Noble during the holiday season. They managed to raise over $400, which we will add to their Walk total. We greatly appreciate their efforts and helping spirit!

More News

More Walk2 cure hemophilia

Special recognition belongs to the winning teams and top fundraisers. The #1 team was "Tag's Turtles," consisting of twenty-two members from the Bowling Green/Glasgow area who raised $3,615.84 under the leadership of Team Captains Monica, Josh, and Tag Poynter. Unfortunately, little Tag in whose honor this team rallied together to fundraise, was in the hospital on the day of our Walk but has since then fully recovered and is doing well. The #2 team was "Mac's Pac" from Frankfort who had thirteen team members and raised $1,505 under the leadership of Team Captain, Alane Foley, in honor of little Maclan Foley. For a second year, "Team Brody" from Owingsville was among the winning teams. In 2014, they came 1st, while this time they placed 3rd. They were also thirteen members strong and raised $1,470 in honor of their Team Captain, young Brody Vanderpool.

The top three winners of personal fundraising efforts either as an individual walker or team member/captain were in 1st place, Pamela Howard with $1,370 raised; in 2nd place, Brody Vanderpool with $1,270; and in 3rd place, Alane Foley with $1,110. Note: These amounts were based on the day of event tally and may have increased subsequently. The event raised $32,000.

Special thanks also to our sponsors, who were Novo Nordisk, CSL Behring, Option Care (Walgreens Infusion Services), CVS Caremark, Emergent BioSolutions, Kosair Charities, Matrix Health, and Republic Bank & Trust Company.

Mark your calendars for October 8th and start raising money for the next KHF Walk.

In Memory

November 1, 2015 – December 31, 2015

Gone from our sight but never our memories; gone from our touch but never our hearts…

William L. Farmer, Sr.
Mrs. William L. Farmer, Sr.
Mrs. William L. Farmer, Sr.
Mrs. William L. Farmer, Sr.

Alan Taylor Hall
Norma & Walter Hall

Regina Loeser
Janet & Bruce Masterson

Kentucky Hemophilia Foundation Donors

Thank You To All Donors For Their Generous Contributions

July 1, 2015 – December 31, 2015

Eva A. Brenner
Chevron Matching Gift Program
David Hasch
Dr. Joseph H. Cieslak
for camp
Harry & Cindy Clegg
Community Foundation of Louisville for
the Zoeller Company
Nancy Dudley
Greg Fiscus
Michael Gatton
in honor of Greg Gatton
Stan Hankins
Roger Harrell/Harrell Locksmith
Brett Herald
Rex Herald
Glen & Deborah Hitt
Carol Huddleston
Curtis & Winnie Jacobs
Kroger Community Rewards
Jack & Susan Leffew
Justin Lindhorst
Don Mattingly
David & Terry Moore
Carol Nord
Keith Peterson
Brittany & Amanda Radice
Rawlings Creative LLC dba Louisville
Web Group
John & Pat Tharp
Clara Wheatley
Woman of Immanuel-Immanuel UCC
Calvin T. Zehnder

KHF Membership 2015 – 2016

We appreciate your involvement and support!

Members, $20-$25
Megan Couch
Susan Geralds
Janet Goff
William Hamilton
Louise Hardaway
James P. Huff
Laci Norman
Dennis Sanders
John Shackelford

Supporting Members, $35
Danny & Maritza Adams
Judy Hayes
in memory of Jason Hayes
Jim & Shannon Hoskins
Mary E. Marasa
Mike Marlier
Don Mattingly
Cory & Whitney Meadows
Mary Ellen Ritchie
in memory of Michael Steven Mattingly

Patron Members, $50
Larry G. Bandy, Sr.
Wanda Bandy
Debrah Barron
Sara Ceresa
Arthur Hackman
David & Leslie Houvenagle
Justin Lindhorst
Al Loeser, Sr.
Keith Peterson
Stacey Powell & Family

Sustaining Members, $100
Barbara Warms Grayson
Fred & Darline Hartman
Thomas & Mary Hendrix
Glen & Deborah Hitt
Vivian Marcum
Lindsay Martin
John & Pat Tharp
Calvin T. Zehnder

Benefactor Members, $250
Charles & Ruth Hall

Champion/Corporate Members, $500
Dr. Joseph H. Cieslak
Louisville Oral Surgery & Dental Implants

Mark Osborne
First Choice Home Infusion

Do The Five

Follow these steps to prevent or reduce complications of bleeding disorders

1. Get an annual comprehensive checkup at a hemophilia treatment center.
2. Get vaccinated – Hepatitis A and B are preventable.
3. Treat bleeds early and adequately.
4. Exercise to protect your joints.
5. Get tested regularly for blood-borne infections.

To find out more about the National Prevention Program developed by the National Hemophilia Foundation in collaboration with the Centers for Disease Control and Prevention (CDC), click on www.hemophilia.org or call toll-free 800-42-HANDI.

KHF neither recommends nor endorses the products in this publication and does not make recommendations concerning treatment regimen for individuals. KHF suggests that you consult your physician or treatment center before pursuing any course of treatment. This publication is for general information only.

Walk2 cure hemophilia KHF

***Walk* 2016 ~ October 8th**

Step up. Start a team and begin your fundraising now.

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Protecting the Most Precious Gift of All

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UNLOCKING YOUR SELF-POTENTIAL

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

ADVATE SUPPORTS YOU BY IMPROVING YOUR PERSONAL INFUSION EXPERIENCE WITH THE BAXJECT III SYSTEM

The reconstitution process with the BAXJECT III system is easier, faster, and designed for you*

- An all-in-one, connected design[1]
- Broad selection of doses, providing opportunities for single-vial options[1]
- One-step activation with fewer steps for **faster** reconstitution—just press, swirl, flip and withdraw*[1,2]
- **Straightforward** pooling process if more than 1 vial is needed—no additional supplies required[1]

1/2 the time

Reconstitute ADVATE in about **half the time***[2]

*As compared with the BAXJECT II needleless transfer device.

Watch the ADVATE with BAXJECT III system reconstitution video and see how it all comes together at **ADVATE.com**

Share your experience using the ADVATE with BAXJECT III system at **www.BAXJECT3Survey.com**

ADVATE [Antihemophilic Factor (Recombinant)] Important Information

Indications

ADVATE is a medicine used to replace clotting factor (factor VIII or antihemophilic factor) 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 following page for Brief Summary of ADVATE full Prescribing Information.

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

Baxalta

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

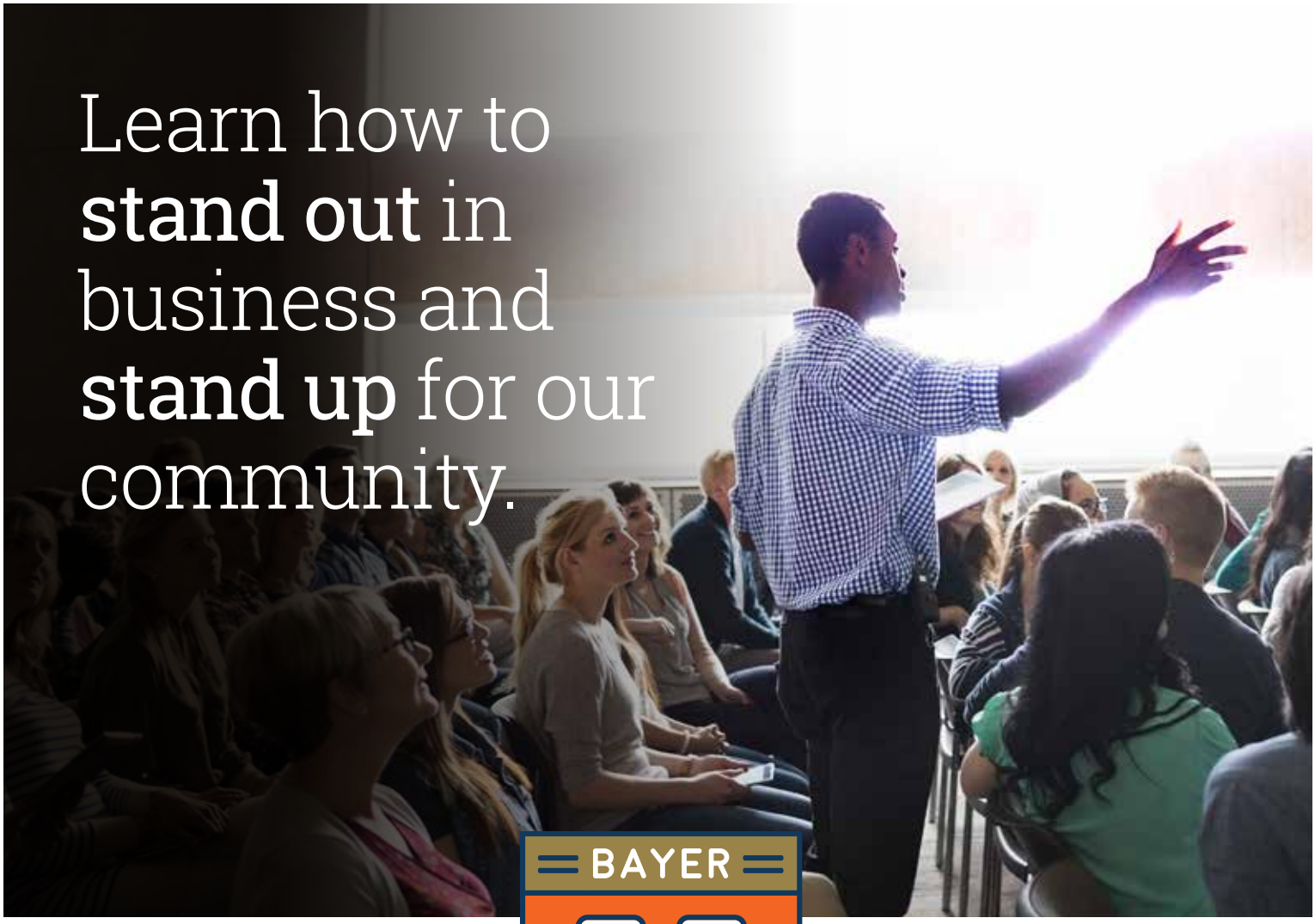
[a] These reactions have been manifested by dizziness, paresthesias, rash, flushing, face swelling, urticaria, and/or pruritus.

Baxter Healthcare Corporation, Westlake Village, CA 91362 USA

U.S. License No. 140 Issued 04/2014

Baxter

Learn how to **stand out** in business and **stand up** for our community.



BAYER

LEADERSHIP

LEADERSHIP BEGINS WITH U

Introducing Leadership U, a **paid** summer **internship*** for full-time college students whose lives have been touched by hemophilia. Work alongside leaders at **Bayer**, while learning how to become a future **leader** in the hemophilia community.

*Includes lodging and transportation costs

ACCEPTING 2016 SUMMER INTERNSHIP APPLICATIONS AT BAYERLEADERSHIPU.COM

Applications are due no later than Friday, February 12, 2016 at 11:59 p.m. ET

Bayer HealthCare

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

ALPROLIX®
[Coagulation Factor IX (Recombinant), Fc Fusion Protein]

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PROTECTION* FROM BLEEDS

Starting with at least a week between prophylaxis infusions

Dosing regimen can be adjusted based on individual response.

*Protection is the prevention of bleeding episodes using a prophylaxis regimen.

To learn more, contact CoRe Manager **Tricia Oppelt** at **tricia.oppelt@biogen.com** or call **585-737-9060**.

INDICATIONS AND IMPORTANT SAFETY INFORMATION

Indications

ALPROLIX, Coagulation Factor IX (Recombinant), Fc Fusion Protein, is a recombinant DNA derived, coagulation factor IX concentrate indicated in adults and children with hemophilia B for:

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

ALPROLIX is not indicated for induction of immune tolerance in patients with hemophilia B.

Important safety information

Do not use ALPROLIX if you are allergic to ALPROLIX or any of the other ingredients in ALPROLIX.

Tell your healthcare provider if you have or have had any medical problems, take any medicines, including prescription and non-prescription medicines, supplements, or herbal medicines, have any allergies and all your medical conditions, including if you are pregnant or planning to become pregnant, are breastfeeding, or have been told you have inhibitors (antibodies) to factor IX.

Allergic reactions may occur with ALPROLIX. Call your healthcare provider or get emergency treatment right away if you have any of the following symptoms: difficulty breathing, chest tightness, swelling of the face, rash, or hives.

Your body can also make antibodies called "inhibitors" against ALPROLIX, which may stop ALPROLIX from working properly.

ALPROLIX may increase the risk of formation of abnormal blood clots in your body, especially if you have risk factors for developing clots.

Common side effects of ALPROLIX include headache and abnormal sensation of the mouth. These are not all the possible side effects of ALPROLIX. Talk to your healthcare provider right away about any side effect that bothers you or does not go away, and if bleeding is not controlled using ALPROLIX.

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 full Prescribing Information on the next page for additional safety information. This information is not intended to replace discussions with your healthcare provider.

ALPROLIX [Coagulation Factor IX (Recombinant), Fc Fusion Protein], Lyophilized Powder for Solution For Intravenous Injection.

FDA Approved Patient Information

ALPROLIX™ /all' pro liks/ [Coagulation Factor IX (Recombinant), Fc Fusion Protein]

Please read this Patient Information carefully before using ALPROLIX™ and each time you get a refill, as there may be new information. This Patient Information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is ALPROLIX™?

ALPROLIX™ is an injectable medicine that is used to help control and prevent bleeding in people with hemophilia B. Hemophilia B is also called congenital Factor IX deficiency.

Your healthcare provider may give you ALPROLIX™ when you have surgery.

Who should not use ALPROLIX™?

You should not use ALPROLIX™ if you are allergic to ALPROLIX™ or any of the other ingredients in ALPROLIX™. Tell your healthcare provider if you have had an allergic reaction to any Factor IX product prior to using ALPROLIX™.

What should I tell my healthcare provider before using ALPROLIX™?

Tell your healthcare provider about all of the medicines you take, including all prescription and non prescription medicines, such as over-the-counter medicines, supplements, or herbal medicines.

Tell your doctor about all of your medical conditions, including if you:

- are pregnant or planning to become pregnant. It is not known if ALPROLIX™ may harm your unborn baby.
- are breastfeeding. It is not known if ALPROLIX™ passes into breast milk or if it can harm your baby.
- have been told that you have inhibitors to Factor IX (because ALPROLIX™ may not work for you).

How should I use ALPROLIX™?

ALPROLIX™ should be administered as ordered by your healthcare provider. You should be trained on how to do infusions by your healthcare provider. Many people with hemophilia B learn to infuse their ALPROLIX™ by themselves or with the help of a family member.

See the Instructions for Use for directions on infusing ALPROLIX™. The steps in the Instructions for Use are general guidelines for using ALPROLIX™. Always follow any specific instructions from your healthcare provider. If you are unsure of the procedure, please ask your healthcare provider.

Do not use ALPROLIX™ as a continuous intravenous infusion.

Contact your healthcare provider immediately if bleeding is not controlled after using ALPROLIX™.

What are the possible side effects of ALPROLIX™?

Common side effects of ALPROLIX™ include headache and abnormal sensation in the mouth.

Allergic reactions may occur. Call your healthcare provider or get emergency treatment right away if you have any of the following symptoms: hives, chest tightness, wheezing, difficulty breathing, or swelling of the face.

ALPROLIX™ may increase the risk of forming abnormal blood clots in your body, especially if you have risk factors for developing blood clots.

Your body can also make antibodies called, "inhibitors," against ALPROLIX™, which may stop ALPROLIX™ from working properly. Your healthcare provider may need to test your blood for inhibitors from time to time.

These are not all the possible side effects of ALPROLIX™. Talk to your healthcare provider about any side effect that bothers you or that does not go away.

How should I store ALPROLIX™?

Store ALPROLIX™ vials at 2°C to 8°C (36°F to 46°F). Do not freeze.

ALPROLIX™ vials may also be stored at room temperature up to 30°C (86°F) for a single 6 month period.

If you choose to store ALPROLIX™ at room temperature:

- Note on the carton the date on which the product was removed from refrigeration.
- Use the product before the end of this 6 month period or discard it. Do not return the product to the refrigerator.
- Do not use product or diluent after the expiration date printed on the carton, vial or syringe.

After Reconstitution:

- Use the reconstituted product as soon as possible; however, you may store the reconstituted product at room temperature up to 30°C (86°F) for up to 3 hours. Protect the reconstituted product from direct sunlight. Discard any product not used within 3 hours after reconstitution.
- Do not use ALPROLIX™ if the reconstituted solution is cloudy, contains particles or is not colorless.

What else should I know about ALPROLIX™?

Medicines are sometimes prescribed for purposes other than those listed here. Do not use ALPROLIX™ for a condition for which it was not prescribed. Do not share ALPROLIX™ with other people, even if they have the same symptoms that you have.

Manufactured by
Biogen Idec Inc.
14 Cambridge Center
Cambridge, MA 02142
U.S. License # 697

Alphanate®

Antihemophilic Factor/von Willebrand Factor Complex (Human)

Physician **Preferred**

ALPHANATE is the **preferred plasma-derived FVIII** product for the treatment of **hemophilia A** among hematologists practicing in HTCs.*

*Results are statistically significant with a 95% confidence interval with a 6.5% margin of error and are based on a blinded national survey of 75 HTC-based Hematologists from a list of federally and non-federally funded HTCs within the US, conducted and validated by a reputable, independent third party, Adivo Associates LLC, on behalf of Grifols USA from October 2014 - January 2015. In order to qualify to complete the survey, Hematologists were rigorously screened according to market research standards having the necessary experience in the relevant treatment segment. Respondents were asked to assume no difference in terms of availability, cost, and reimbursement when indicating their most preferred plasma-derived FVIII brand.

HTC=Hemophilia Treatment Center; pdFVIII=plasma-derived factor VIII

Learn more at **alphanate.com**

Indications

ALPHANATE® (antihemophilic factor/von Willebrand factor complex [human]) is indicated for:

- Control and prevention of bleeding in patients with hemophilia A
- Surgical and/or invasive procedures in adult and pediatric patients with von Willebrand disease (VWD) in whom desmopressin (DDAVP®) is either ineffective or contraindicated. It is not indicated for patients with severe VWD (Type 3) undergoing major surgery

Important Safety Information

ALPHANATE is contraindicated in patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components.

Anaphylaxis and severe hypersensitivity reactions are possible. Should symptoms occur, treatment with ALPHANATE should be discontinued, and emergency treatment should be sought.

Development of activity-neutralizing antibodies has been detected in patients receiving FVIII containing products. Development of alloantibodies to VWF in Type 3 von Willebrand disease (VWD) patients has been occasionally reported in the literature.

Thromboembolic events may be associated with AHF/VWF Complex (Human) in VWD patients, especially in the setting of known risk factors.

Intravascular hemolysis may be associated with infusion of massive doses of AHF/VWF Complex (Human).

Rapid administration of a FVIII concentrate may result in vasomotor reactions.

Plasma products carry a risk of transmitting infectious agents, such as viruses, and theoretically, the Creutzfeldt-Jakob disease (CJD) agent, despite steps designed to reduce this risk.

The most frequent adverse events reported with ALPHANATE in >5% of patients are respiratory distress, pruritus, rash, urticaria, face edema, paresthesia, pain, fever, chills, joint pain, and fatigue.

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

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.

For more information: **Grifols Biologicals Inc.**
Tel. 888-GRIFOLS (888-474-3657)

Grifols Biologicals Inc.
5555 Valley Boulevard, Los Angeles, 90032 CA - USA Tel. 888-GRIFOLS (888 474 3657)
www.grifols.com

GRIFOLS

Come Walk with Us

Put together your team and start raising money now!

Kentucky Hemophilia Walk

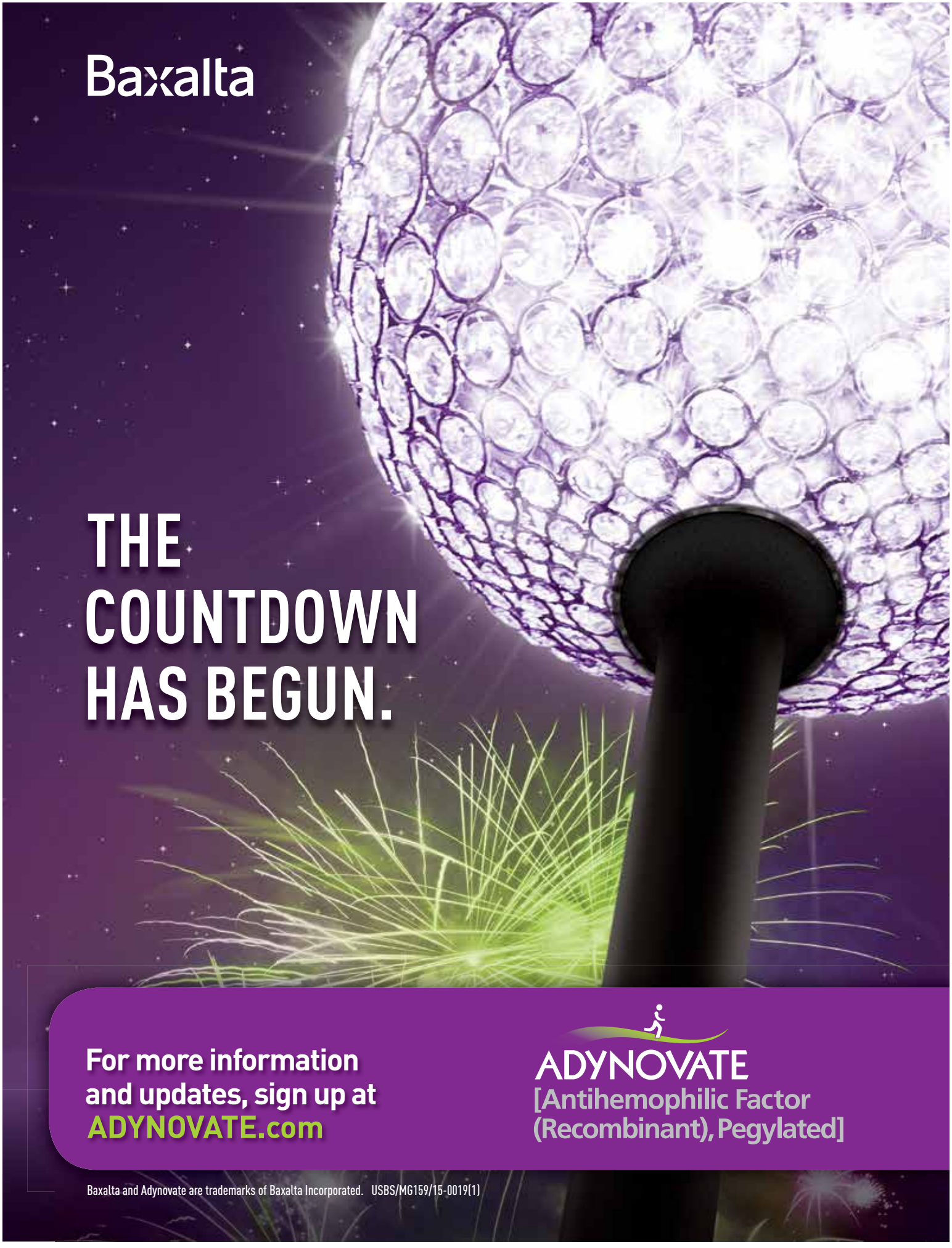
Saturday, October 8
Wetherby Park, Middletown KY

Be a step ahead. October will be here before you know it. Go ahead and start planning your ***Walk*** strategy now.

Winning Teams get all sorts of cool prizes while they raise money for a great cause. Plus, we have tons of fun.

Walk2 cure hemophilia KHF

email: walk@kyhemo.org
502-456-3233
800-582-CURE (2873)


Baxalta
THE COUNTDOWN HAS BEGUN.
For more information and updates, sign up at ADYNOVATE.com
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[Antihemophilic Factor (Recombinant), Pegylated]
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