FALL 2013

Rocky Mountain Hemophilia & Bleeding Disorders Association

RMHBDA Newsletter

The Rocky Mountain

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

RMHBDA Education Weekend 2014

April 4–6

Our Education Weekend will take place at the Best Western Grand Northern Hotel in Helena,Montana.

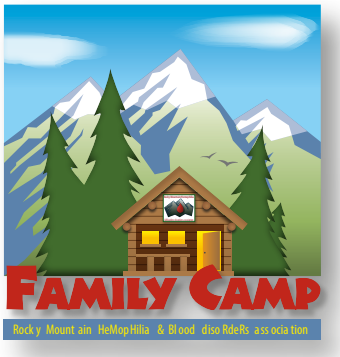
We need help organizing!

Please contact Brad at 406.600.2554 if you are interested in serving on the Education Weekend committee. This is your organization!

Family Camp 2014

June 20–22

Camp on the Boulder, McLeod, MT
For more information,
visit www.campontheboulder.org/



Each summer, RMHBDA invites affected families living in Montana and Wyoming to attend a weekend retreat. The weekend is packed full of education, bonding, and fun!

For the parents and teens, we will have team building programming led by our guest, hemophilia leadership expert, Pat Torrey (www.pattorrey.com) and some time to relax with other families. This is a great opportunity to learn from and share experiences with one another.

We also have many great activities planned for our campers including arts & crafts projects, field games, and educational sessions for children with bleeding disorders and their siblings. Infusion classes will be offered from our HTC

Call Brad with any questions at 406.586.4050

From Our Executive Director

We couldn't have asked for a nicer day on September 7, 2013. We had over 150 walkers at our **Second Annual Walk for Hemophilia** *at Bogert Park in Bozeman, Montana. Good natured and generous supporters helped raise over $44,000 and awareness at our second ever walk. I want to send a very gracious thank you to our volunteers, team captains, and walkers for making our walk a tremendous success. We are so grateful for your participation.*

We would also like to extend a very gracious thank you to our local and corporate sponsors: St. Vincent's Healthcare, Barnard Construction, Baxter, Bayer, Biogen Idec, Bozeman Deaconess Health Services, CSL Behring, Fifth Street Design, First Interstate Bank, Grifols, HF Healthcare, Insty Prints, Fuller Family Medicine, Walmart, Novo Nordisk, Pfizer, CVS Caremark, *and* Restore RX.

Check our Facebook page for wonderful photos from our walk.

Sincerely,
Brad Benne,
Executive Director

Congratulations On A Successful Walk!

Walk Photos

The second annual RMHBDA Walk was a remarkable success raising over $44,000 and raising awareness of RMHBDA and of blood disorders and safety to the public. It was also wonderful fun with a great turnout as you can see on these pictures (more at facebook.com/rmhbda).

We Also Wish To Honor And Thank Our Top Fundraisers And Teams!

Top Fundraisers

1. John & Will Benne
2. Kristal Graham
3. Chris Graham
4. Campbell Hunter
5. Dylan Hunter
6. Jaxon Stafford
7. Lisa Maxwell
8. Jodi Rudell
9. Craig Akers
10. Scott Maxwell
11. Jessica Amende
12. Silent Donor
13. Ben Kuss
14. Forrest Berg
15. Spencer Straub
16. Connor Ferriter
17. Silent Donor
18. Scott Sears
19. Jaime Nelson
20. Jane Robertson

Top Teams

1. Ty's Crew
2. Blood Brothers II
3. The Warriors
4. Best of the Bleed
5. Max Bleeders
6. Wyo Red's
7. The VW Ladybugs Plus One
8. The Infusing Four
9. Clot Like an Amende
10. Activate to coagulate
11. Connor's Comrades
12. Hart Genug Zu Bluten
13. Wyoming Willebrand Walkers
14. St. Vincent Children's Cancer and Blood Disorders
15. Carter's Carriers
16. Bleeding Besties
17. Clot Trotters
18. Walgreens Infusion Services
19. Accredo
20. Pfi er













See many more and larger versions at

www.facebook.com/rmhbda

Access to Pediatric Specialists "Really Big Deal" for Parents of Hemophiliac Child

Billings Gazette, September 25, 2013 by Cindy Uken

Scraped knees and elbows, bruises and scabs are a rite of passage for most 6-year-old boys.

For Ty Graham and his parents, Chris and Jana Graham, these routine childhood traumas are the cause of signifi ant concern.

The first grader at Arrowhead Elementary was born with hemophilia, an inherited bleeding disorder that prevents the blood from clotting properly. He was diagnosed at birth. About 400 babies — mostly boys — are born with hemophilia each year in the United States. An estimated 40 children in Montana have been diagnosed with the disorder.

"Initially, we were terrifie ," said Chris Graham, a physician assistant at St. Vincent Healthcare.

The lifelong disorder can result in bleeding within joints that can lead to chronic joint disease and pain; bleeding in the head and sometimes in the brain, which can cause long-term problems such as seizures and paralysis; and death if the bleeding cannot be stopped or if it occurs in a vital organ such as the brain.

Until now, the Graham family — and others like them — might have had to seek treatment in Denver, but no longer. About a year ago, St. Vincent Healthcare brought on staff Dr. Carrie Neuhardt, a pediatric hematologist-oncologist. She is part of a team of pediatric specialists that St. Vincent Healthcare has amassed as it positions itself to build what one day could be called the Montana-Northern Wyoming Children's Hospital.

St. Vincent Healthcare and the St. Vincent Healthcare Foundation are putting their commitment to building pediatric specialty services on center stage at the 35th Annual SAINTS Ball, the foundation's premier fundraising event. The Oct. 5 event is expected to raise more than $1 million to support and expand pediatric intensive and specialty care services at the hospital.

At times, Ty has had to forgo recess, T-ball and even classes because of bleeding episodes. His vacation time has also occasionally been affected.

"It stinks to be the dorky kid who has to sit out of PE class," said Jana Graham.

As difficult as it can be on Ty, hemophilia has been emotionally taxing on his parents. Babies, especially when they begin crawling, and active children with hemophilia, bruise easily. Sometimes the bruises appear in unlikely places such as the child's stomach, chest, buttocks and back. Ty's parents were warned early on they may be suspected of child abuse.

The possibility of such claims still triggers an emotional response in the mother of three.

"It used to be a huge, horrific nightmare for us," Jana said.

In May, Ty started prophylactic injections, infusing himself three times each week with a clotting agent that the body does not produce naturally. Each infusion takes about 15minutes and retails for $25,000.

"Besides getting shots, he's a normal little boy," said his father. "The world is open to him."

Having ready access to a pediatric hematologist is signifi ant in helping keep the disorder in check, Chris said.

Jana Graham holds the box of syringes and blood-clotting medication that her 6-year-old son Ty uses to control his hemophilia. Ty injects himself with the clotting agent three times each week. Ty was born with hemophilia, a disorder in which the blood does not clot properly. He inherited it from his mother.

"It's a really big deal, especially when it comes to your kids," Jana said. "To have someone who can take care of them locally is huge."

The key to treating hemophilia is access to care, Neuhardt said. That involves educating the family on the disorder, keeping families together in the state and reducing the stress often associated with the disorder. The overriding goal is to do whatever possible to let children lead normal lives.

"This is gold-standard care, the same quality care offered at a larger facility — but with a personalized touch."

Chris Graham will attest to the personalized touch. He has Neuhardt's personal cellphone number — as do others. He knows he can call her day or night.

"These are serious diseases," Neuhardt said. "If you can make a family feel better, that's a small thing to do."

As for Ty, he describes it all simply as "weird." A Medic Alert bracelet around his tiny wrist is a constant reminder of the weirdness.

"I don't really feel anything," he said. "I like being thrown around and playing with my shield and sword."

He roller skates and rides an electric scooter. He just returned with his family from biking the Hiawatha Trail. He also enjoys swimming.

And, for good measure, he said, "I like driving my sisters crazy."

Original article in the Billings Gazette at http://goo.gl/QV6EMA

NOW APPROVED

NEW RIXUBIS [COAGULATION FACTOR IX (RECOMBINANT)]

A recombinant factor IX indicated for routine prophylaxis to treat adults with hemophilia B[1]

Available FALL 2013

For more information, contact your Baxter representative today:

Steve McKell
Phone: (801) 395-4670
E-mail: steve_mckell@baxter.com

To learn more, visit www.RIXUBIS.com

Indications for RIXUBIS [Coagulation Factor IX (Recombinant)]

RIXUBIS is an injectable medicine used to replace clotting factor IX that is missing in people with hemophilia B (also called congenital factor IX deficiency or Christmas disease).

RIXUBIS is used to prevent and control bleeding in adults with hemophilia B. Your healthcare provider may give you RIXUBIS when you have surgery. RIXUBIS can reduce the number of bleeding episodes in adults when used regularly (prophylaxis).

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

Detailed Important Risk Information for RIXUBIS [Coagulation Factor IX (Recombinant)]

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

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 hamsters, are nursing, are pregnant or planning to become pregnant, or have been told that you have inhibitors to factor IX.

You can have an allergic reaction to RIXUBIS. Call your healthcare provider or get emergency treatment right away 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 IX. An inhibitor is part of the body's defense system. If you form inhibitors, it may stop RIXUBIS 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 IX.

If you have risk factors for developing blood clots, the use of factor IX products may increase the risk of abnormal blood clots.

Some common side effects that have been reported with RIXUBIS include: unusual taste in the mouth and limb pain.

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

Please see Brief Summary of RIXUBIS Prescribing Information on following 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.

Reference: 1. RIXUBIS [Prescribing Information]. Westlake Village, CA: Baxter Healthcare Corporation; June 2013.

Baxter

RIXUBIS [Coagulation Factor IX (Recombinant)]
For Intravenous Injection
Brief Summary of Prescribing Information: Please see package insert for full Prescribing Information.

INDICATIONS AND USAGE

Control and Prevention of Bleeding Episodes

RIXUBIS [Coagulation Factor IX (Recombinant)] is an antihemophilic factor indicated for control and prevention of bleeding episodes in adults with hemophilia B.

Perioperative Management

RIXUBIS is indicated for perioperative management in adults with hemophilia B.

Routine Prophylaxis

RIXUBIS is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults with hemophilia B.

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

CONTRAINDICATIONS

RIXUBIS is contraindicated in patients with:

- Known hypersensitivity to RIXUBIS or its excipients including hamster protein
- Disseminated intravascular coagulation (DIC) [see *Warnings and Precautions*]
- Signs of fibrinolysis [see *Warnings and Precautions*]

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have been reported with factor IX-containing products. The risk is highest during the early phases of initial exposure to factor IX concentrates in previously untreated patients (PUPs), in particular in patients with high-risk gene mutations. Early signs of allergic reactions, which can progress to anaphylaxis, include angioedema, chest tightness, hypotension, lethargy, nausea, vomiting, paresthesia, restlessness, wheezing, and dyspnea. Immediately discontinue administration and initiate appropriate treatment if allergic- or anaphylactic-type reactions occur. In case of severe allergic reactions, alternative hemostatic measures should be considered.

There have been reports in the literature showing an association between the occurrence of a factor IX inhibitor and allergic reactions. Evaluate patients experiencing allergic reactions for the presence of an inhibitor.

RIXUBIS contains trace amounts of Chinese hamster ovary (CHO) proteins. Patients treated with this product may develop hypersensitivity to these non-human mammalian proteins.

Inhibitors

Evaluate patients regularly for the development of factor IX inhibitors by appropriate clinical observations and laboratory tests. Perform an assay that measures factor IX inhibitor concentration if expected factor IX activity plasma levels are not attained, or if bleeding is not controlled with an expected dose. Contact a specialized hemophilia treatment center if a patient develops an inhibitor.

Patients with factor IX inhibitors are at an increased risk of severe hypersensitivity reactions or anaphylaxis if re-exposed to RIXUBIS. RIXUBIS may not be effe tive in patients with high titer factor IX inhibitors and other therapeutic options should be considered.

Nephrotic Syndrome

Nephrotic syndrome has been reported following attempted immune tolerance induction in hemophilia B patients with factor IX inhibitors. The safety and effic y of using RIXUBIS for immune tolerance induction have not been established.

Thromboembolic Complications

The use of factor IX containing products has been associated with the development of thromboembolic complications (e.g., pulmonary embolism, venous thrombosis, and arterial thrombosis). Due to the potential risk for thromboembolic complications, monitor patients for early signs of thrombotic and consumptive coagulopathy, when administering RIXUBIS to patients with liver disease, with signs of fibrinolysi , peri- and post-operatively, or at risk for thrombotic events or DIC. The benefit of t eatment with RIXUBIS should be weighed against the risk of these complications in patients with DIC or those at risk for DIC or thromboembolic events.

Monitoring Laboratory Tests

- Monitor factor IX activity plasma levels by the one-stage clotting assay to confirm th t adequate factor IX levels have been achieved and maintained [see *Dosage and Administration in full Prescribing Information*].
- Monitor for the development of inhibitors if expected factor IX activity plasma levels are not attained, or if bleeding is not controlled with the recommended dose of RIXUBIS. Assays used to determine if factor IX inhibitor is present should be titered in Bethesda Units (BUs).

ADVERSE REACTIONS

The most common adverse reactions observed in >1% of subjects in clinical studies were dysgeusia, pain in extremity, and positive furin antibody test.

Clinical Trials Experience

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

During clinical development, in a combined study, 91 male previously treated patients (PTPs; exposed to a factor IX-containing product for ≥150 days) received at least one infusion of RIXUBIS as part of either on-demand treatment of bleeding episodes, perioperative management of major and minor surgical, dental, or other invasive procedures, routine prophylaxis, or pharmacokinetic evaluation of RIXUBIS. Six subjects (6.6%) were <6 years of age, 10 (11%) were 6 to <12 years of age, 3 (3.3%) were adolescents (12 to <16 years of age), and 72 (79%) were adults (16 years of age and older). The subjects received a total of 7,353 infusions with a median of 85 infusions of RIXUBIS (range 3 to 212 infusions), for a median of 83 exposure days (range 83 to 209 days).

A total of 161 adverse events were reported in 48 (52.7%) of the 91 subjects. Adverse reactions that occurred in >1% of subjects are shown in Table 3.

Table 3: Summary of Adverse Reactions

System Organ Class	Adverse Reactions (AR)	Number of ARs (N)	Number of Subjects (N=91) n (%)	Percent per Infusion (N=7353)
Nervous System Disorders	Dysgeusia	2	1 (1.1%)	0.03%
Musculoskeletal and Connective Tissue Disorders	Pain in extremity	1	1 (1.1%)	0.01%
Investigations	Positive furin antibody test[a]	1	1 (1.1%)	0.01%
	Factor IX or furin antibodies of indeterminate specifici y[a]	9	7 (7.7%)	0.12%

[a]See Immunogenicity.

Immunogenicity

All 91 subjects were monitored for inhibitory and binding antibodies to factor IX, and binding antibodies to CHO protein and furin, at the following time points: at screening, at 72 hours following the first infusion of RIXUBIS and the ommercial recombinant factor IX product in the cross-over portion of the pharmacokinetic study, after 5 and 13 weeks following first xposure to RIXUBIS, and thereafter every 3 months. Antibodies against furin were tested by an in-house enzyme-linked immunosorbent assay (ELISA). A titer of 1:20 or 1:40 was considered to be indeterminate for the above validated assay, as these titers were too low to be verified y the confirm tory assay.

No subjects developed neutralizing antibodies to factor IX. Thirteen subjects (14.3%) developed low-titer, non-neutralizing antibodies against factor IX at one or more time points. Two of these 13 subjects were found to have these antibodies at screening, prior to receiving RIXUBIS. No clinical adverse findings ere observed in any of these 13 patients.

Thirteen subjects (14.3%) had signals for antibodies against furin (indeterminate specifici y). Four of these 13 subjects expressed signals for antibodies at screening, prior to RIXUBIS treatment. An additional subject had an antibody signal after treatment with the comparator product and prior to RIXUBIS treatment. Another additional subject had a positive titer of 1:80 that was not present when checked at a later time point and therefore considered transient. A second subject had a positive antibody signal after the data cutoff d te that was also transient. No clinical adverse findings ere observed in any of these 15 patients.

In a study of 500 normal volunteers, using the same assay as in the clinical trial, 7% had titers of 1:20 or 1:40 and 1.2% had higher titers ranging from 1:80 to 1:320. These antibodies are thought to be part of a natural immune system response. To date, these antibodies have not been associated with any clinical adverse finding .

The detection of antibody formation is highly dependent on the sensitivity and specifici y of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influen ed by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease.

Thrombogenicity

There was no clinical evidence of thromboembolic complications in any of the subjects. Out-of-range values for thrombogenicity markers (thrombin-antithrombin III, prothrombin fragment 1.2, and D-dimer), determined during the pharmacokinetic portion of the combined study, did not reveal any pattern indicative of clinically relevant thrombogenicity with either RIXUBIS or a comparator factor IX-containing product.

Post-marketing Experience

Because the following 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.

No post-marketing adverse reactions have been reported with RIXUBIS.

The following class adverse reactions have been seen with another recombinant factor IX: inadequate factor IX recovery, inhibitor development, anaphylaxis, angioedema, dyspnea, hypotension, and thrombosis.

Baxter Healthcare Corporation, Westlake Village, CA 91362 USA
U.S. License No. 140 Issued JUN 2013
BIOH0305

Baxter

Having issues with co-pays or gaps in coverage for your **hemophilia A** treatment ???

We may be able to help.

Bayer offers a range of programs that can help you **navigate insurance questions about your hemophilia A** treatment. If you're having issues with co-pays or gaps in coverage, we may be able to offer assistance. Speak with one of our case specialists to find out more.

Call **1-800-288-8374** and press 1 to speak to a trained **insurance specialist!**

Ladies Only: RMHBDA's "Women's Escape"

Friday –Sunday
November 8–10,2013
Chico Hot Springs, Pray, MT

We need to organize! Please contact Brad if you are interested in attending and planning our program. Ladies, please leave the boys at home.

Our Women's Escape committee includes: Jessica Amende, Christy Savage, Heidi Hart, Jane Robertson, and Sara Jestrab. Thank you for your time and support in planning this event. **All of your expenses at Chico Hot Springs will be covered**. If you need fuel assistance, please talk with Brad.

VICTORY FOR WOMEN
WITH BLOOD DISORDERS
WWW.VICTORYFORWOMEN.ORG

Please RSVP
Brad Benne
brad.rmhbda@gmail.com
(406) 586-4050

Dr. Feist of Bozeman Deaconess Retires

I would like to announce my retirement from Bozeman Deaconess Health Group Pediatrics effective September 1, 2013.It has been a wonderful privilege caring for your children the past 36 years. We have six pediatricians in our practice who will continue to care for your children and I encourage you to call the office at 587-5123to schedule your next appointment.

As Dr. Seuss would say:

"Oh, the places you'll go, there is fun to be done . . .
You're off to great places, today is your day!
Your mountain is waiting, so . . . get on your way!"

Novo Nordisk's HERO Presentation

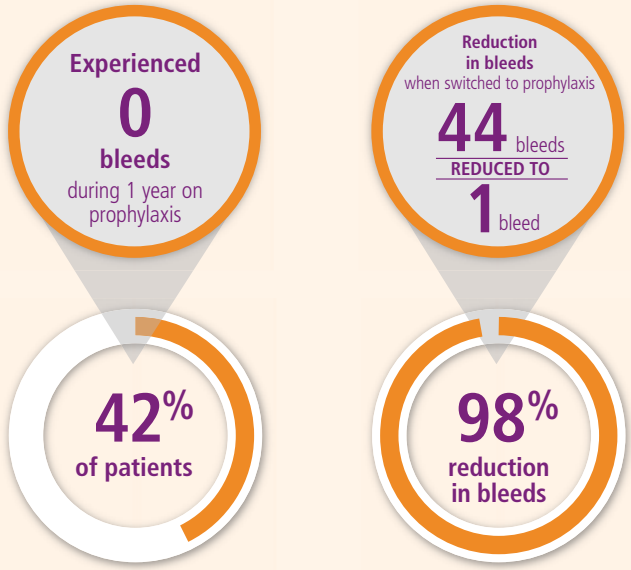
On September 6, 2013,over 20 people attended Novo Nordisk's HERO presentation at the Baxter Hotel in Bozeman, Montana. We were fortunate to have our former HTC RN, Sue Geraghty present to our group. A special thank you to Sherry McLendon and Novo Nordisk for sponsoring the event. Sue shared valuable information and her extensive experiences as a medical professional with our chapter.

UNLOCKING SELF-POTENTIAL

PROPHYLAXIS WITH ADVATE REDUCED BLEEDS IN A CLINICAL STUDY[1,a]

ADVATE is the only recombinant factor VIII (eight) that is FDA approved for prophylaxis in both adults & children (0-16 years)[1]

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



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

[a]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 with severe or moderately severe hemophilia A.

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

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.

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 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.

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

References:

1. ADVATE Prescribing Information. Westlake Village, CA: Baxter Healthcare Corporation; July 2012. **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), Plasma/Albumin-Free Method]
There's more to life.

www.advate.com | 888.4.ADVATE

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 information]*

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 (5.3) in full prescribing information]*

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 muIgG protein antibodies. Of these, 10 showed an upward trend in anti-muIgG 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 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 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] 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.

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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Tentative 2014 Program & Event Calendar

As of October 1, 2013. The chapter is still determining exact dates for: Men's Retreat in potential conjunction with Snake River Hemophilia Association, and CSL's Getting in the Game Program.

January
- NHF National Walk Training: January 12-14
- NACCHO Camp Conference: January 24-26

February
- NHF Washington Days: February 26-28
- Men's Retreat in Bozeman or West Yellowstone (TBD)

March
- Hemophilia Awareness Month!
- HFA Annual Symposium: March 27-30

April
- RMHBDA Education Weekend in Helena: April 4-6
- World Hemophilia Day: April 17

May
- Education Series/Walk "Call to Action" Meeting (Bozeman, Billings, Helena) TBD

June
- RMHBDA Family Camp (Camp on the Boulder, McLeod, MT): June 20-22

July
- Mile High Summer Camp Leadership Pre-camp Retreat: July 11-13
- Mile High Summer Camp (Rocky Mountain Village, Empire CO): July 13-18

August
- Walk Kickoff Event in Bozeman, Billings, Helena (TBD)

September
- RMHBDA Walk for Hemophilia (Bozeman): Pending per MSU football schedule and park availability.
- NHF Annual Meeting (Washington, D.C.): September 18-20
- CSL Gettin In the Game (TBD)

2013 Mile High Colorado Camp

A Powerful and Meaningful Experience

I had the honor of attending Mile High Camp this year and the experience changed my life. The opportunity each camper encounters is empowering and life-changing. I want every kid dealing with bleeding disorders in Montana and Wyoming to experience Mile High Camp.

Stay tuned for information about next year's camp in March of 2014!

Advocacy It's In Your Blood

This afternoon HFA, along with other members from the Coalition for Accessible Treatments (CAT), held a briefing on Capitol Hill to release a study of the impact of H.R. 460, the **Patient's Access to Treatments Act of 2013**, a bill that protects access to medically necessary treatments for patients with chronic conditions, like hemophilia and other bleeding disorders.

According to the study conducted by Avalere Health, H.R. 460 would have a negligible effect on insurance premiums, increasing premium costs by only an average of $3 per year for plans with specialty tiers.

The Patients' Access to Treatments Act establishes cost-sharing limits for health plans that cover prescription drugs and use a formulary or other tiered cost-sharing structure. The Act prohibits insurance companies from imposing cost-sharing requirements, including co-payment and co-insurance, on drugs in a specialty tier that are higher than the cost-sharing requirements of drugs in non-preferred brand tiers. If a plan uses more than one non-preferred brand tier, then they must use the tier where the cost sharing is lowest.

Hemophilia Federation of America

Over the past year, HFA has been involved with CAT, a coalition of numerous patient advocacy organizations, working hard to gather support for the passage of this bill. This bill is extremely important for the bleeding disorders community as it will ensure that the high cost of factor, a drug that does not have a generic alternative, cannot be passed onto patients through high, percentage based co-pays.

HFA will continue to keep you updated about the progress of H.R. 460. In the meantime, you can contact your member of Congress and tell him/her about the importance of this legislation and a personal story on how your life would be impacted if your health insurance included coverage of factor, or other specialty medication, on a specialty tier.

FDA Grants Orphan Drug Status to Alnylam's Hemophilia Therapy

Sources: The Wall Street Journal, August 14,2013,and Alnylam news release dated August 20, 2013

In August, Alnylam Pharmaceuticals, Inc., announced that the US Food and Drug Administration (FDA) had granted Orphan Drug Designation to ALN-AT3 for the treatment of hemophilia A. The company, based in Cambridge, Massachusetts, is developing ALN-AT3, a subcutaneously administered (injection just under the skin) RNAi therapy that targets antithrombin (AT) as a way to treat hemophilia A or B, hemophilia A or B with inhibitors, and other rare bleeding disorders. AT is a small plasma protein molecule that inactivates factor Xa and thrombin, which are needed for blood clotting.

ALN-AT3 incorporates Alnylam's proprietary gene-silencing technology called RNAi, or RNA interference. Discovered by scientists in the late 1990s, RNAi is a natural process in which cells turn off, or silence, the activity of specific genes. ALN-AT3 silences certain genes associated with AT generation, "switching off" the protein's production.

At the XXIV Congress of the International Society on Thrombosis and Haemostasis, June 29-July 4, in Amsterdam, Alnylam shared preclinical data from animal trials. The studies revealed that ALN-AT3 improved thrombin generation in mice and nonhuman primates.

Alnylam plans to file an investigational new drug application for ALN-AT3 in late 2013.It will initiate a Phase I clinical trial in humans in early 2014.

"We are very pleased that the FDA has granted Orphan Drug Designation for ALN-AT3 now for both the treatment of hemophilia A and hemophilia B. As a subcutaneously delivered RNAi therapeutic, we believe it represents an innovative approach for the management of hemophilia and has great potential to make a meaningful impact in the treatment of this often debilitating bleeding disorder," said Saraswathy (Sara) Nochur, PhD, Senior Vice President, Regulatory Affair and Quality Assurance at Alnylam. "ALN-AT3 is a key program in our 'Alnylam 5x15' product development and commercialization strategy, and we look forward to advancing this promising RNAi therapeutic into the clinic in the months to come."

Short Survey

Parental Disclosure of Hemophilia Carrier Status to Daughters

My name is Katharine Bisordi and I am currently a genetic counseling student at the University of Maryland. I would like to invite you to participate in my graduate thesis research project.

The study I am conducting is investigating the factors that influen e parents' decision to disclose certain or potential carrier status to daughters in families with hemophilia. Though the literature does contain some information about attitudes towards carrier testing, the factors that influen e parental disclosure of carrier status to their daughters remain to be described in detail. Further investigation of these factors would not only fill a void in the literature, but also aid genetic counselors and health practitioners in future counseling of these families.

The online survey should take approximately 15–20minutes to complete. When the survey has been completed, you will be able to submit it online. The survey will remain open until October 31,2013.You can access the survey at www.surveymonkey.com/s/hemophiliastudy

Thank you for taking the time to complete the survey and aid in my graduate research project. Your participation is very highly valued and appreciated, and also necessary for the collection of data and completion of this study. Please feel free to contact me with any questions you may have.

Sincerely, Katharine Bisordi, BS, MS
Candidate for Master's in Genetic Counseling, University of Maryland School of Medicine
Katharine.Bisordi@som.umaryland.edu

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