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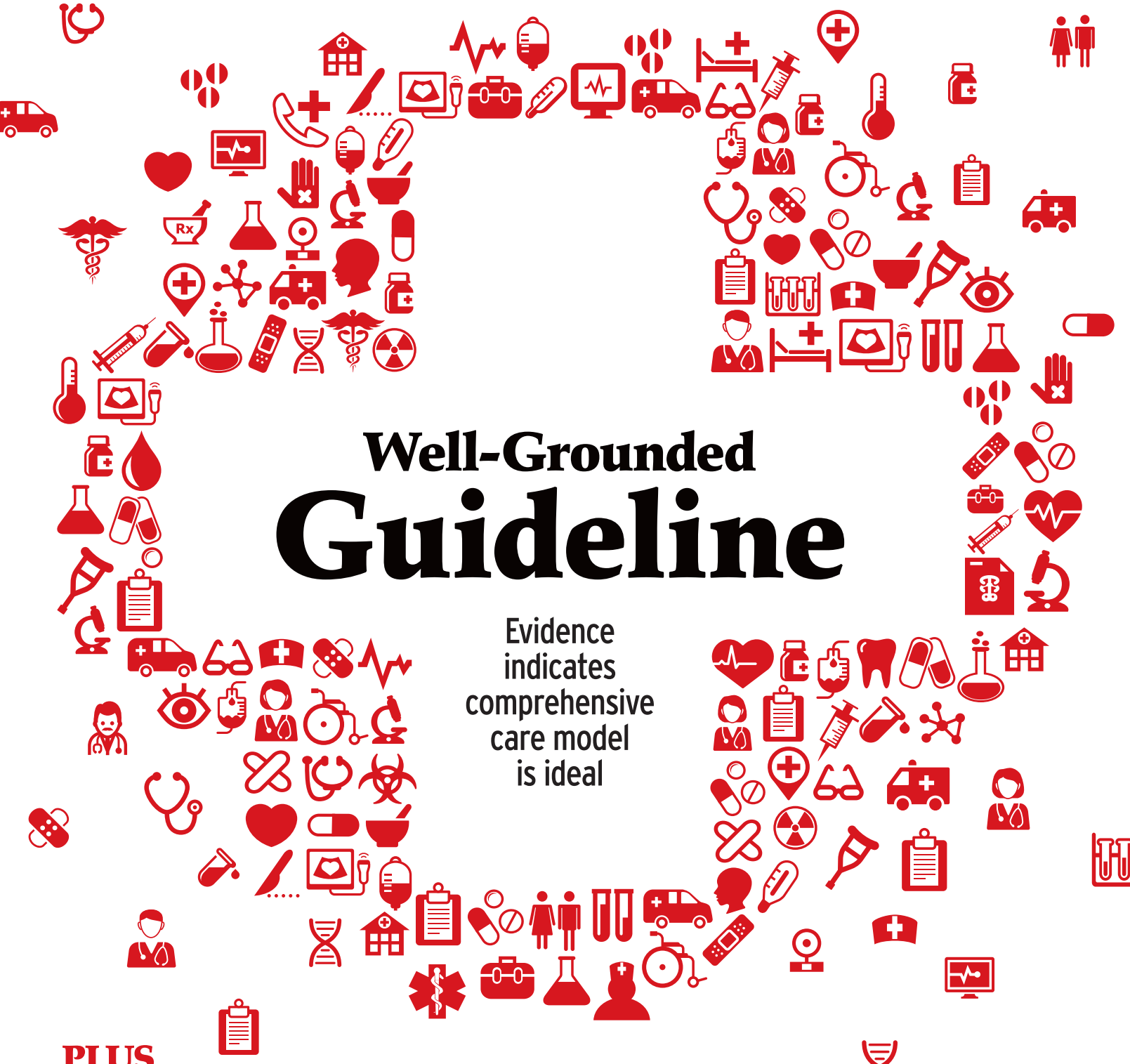
National Hemophilia Foundation

HEMAWARE[SM]

The Bleeding Disorders Magazine



Well-Grounded Guideline

Evidence indicates comprehensive care model is ideal

PLUS

Parcourse Workout | Changes to Medicaid | Liver Follow-up

Fall 2016
Vol 21 • Issue 4

Please see the following brief summary of full prescribing information on the adjacent page, and the full prescribing information, including patient product information, at AFSTYLA.com.

Biotherapies for Life® **CSL Behring**

For adults and children with hemophilia A

REACH HIGHER

With the Long-lasting Protection of AFSTYLA

AFSTYLA is the first and only recombinant Factor VIII that delivers proven, long-lasting bleed protection with a novel single-chain design

2x WEEKLY AVAILABLE

FDA-approved for dosing 2 or 3 times a week

ZERO BLEEDS (median AsBR*)

In clinical trials, whether dosed 2 or 3 times a week

COMPARABLE TO NATURAL FACTOR VIII

Identical to natural Factor VIII once activated

Zero inhibitors observed—Low incidence of side effects in clinical trials

In clinical trials, dizziness and allergic reactions were the most common side effects.

Visit AFSTYLA.com to sign up for the latest news

*Annualized spontaneous bleeding rate in clinical trials (interquartile range [IQR]=0–2.4 for patients ≥12 years; 0–2.2 for patients <12 years).

Important Safety Information

AFSTYLA is used to treat and control bleeding episodes in people with hemophilia A. Used regularly (prophylaxis), AFSTYLA can reduce the number of bleeding episodes and the risk of joint damage due to bleeding. Your doctor might also give you AFSTYLA before surgical procedures.

AFSTYLA is administered by intravenous injection into the bloodstream, and can be self-administered or administered by a caregiver. Your healthcare provider or hemophilia treatment center will instruct you on how to do an infusion. Carefully follow prescriber instructions regarding dose and infusion schedule, which are based on your weight and the severity of your condition.

Do not use AFSTYLA if you know you are allergic to any of its ingredients, or to hamster proteins. Tell your healthcare provider if you previously had an allergic reaction to any product containing Factor VIII (FVIII), or have been told you have inhibitors to FVIII, as AFSTYLA might not work for you. Inform your healthcare provider of all medical conditions and problems you have, as well as all medications you are taking.

Immediately stop treatment and contact your healthcare provider if you see signs of an allergic reaction, including a rash or hives, itching, tightness of chest or throat, difficulty breathing, lightheadedness, dizziness, nausea, or a decrease in blood pressure.

Your body can make antibodies, called inhibitors, against FVIII, which could stop AFSTYLA from working properly. You might need to be tested for inhibitors from time to time. Contact your healthcare provider if bleeding does not stop after taking AFSTYLA.

In clinical trials, dizziness and allergic reactions were the most common side effects. However, these are not the only side effects possible. Tell your healthcare provider about any side effect that bothers you or does not go away.

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.

AFSTYLA®
Antihemophilic Factor (Recombinant), Single Chain

AFSTYLA®, Antihemophilic Factor (Recombinant), Single Chain
For Intravenous Injection, Powder and Solvent for Injection
Initial U.S. Approval: 2016

BRIEF SUMMARY OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use AFSTYLA safely and effectively. Please see full prescribing information for AFSTYLA, which has a section with information directed specifically to patients.

What is the most important information I need to know about AFSTYLA?

- Your healthcare provider or hemophilia treatment center will instruct you on how to do an infusion on your own.
- Carefully follow your healthcare provider's instructions regarding the dose and schedule for infusing this medicine.

What is AFSTYLA?

- AFSTYLA is a medicine used to replace clotting Factor VIII that is missing in patients with hemophilia A.
- Hemophilia A is an inherited bleeding disorder that prevents blood from clotting normally.
- Does not contain human plasma derived proteins or albumin.
- Your healthcare provider may give you this medicine when you have surgery.
- Is used to treat and control bleeding in all patients with hemophilia A.
- Can reduce the number of bleeding episodes when used regularly (prophylaxis) and reduce the risk of joint damage due to bleeding.
- Is not used to treat von Willebrand disease.

Who should not use AFSTYLA?

You should not use AFSTYLA if you:

- Have had a life-threatening allergic reaction to it in the past.
- Are allergic to its ingredients or to hamster proteins.

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

What should I tell my healthcare provider before using AFSTYLA?

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 hamster proteins.
- Have been told you have inhibitors to Factor VIII (because this medicine may not work for you).

How should I use AFSTYLA?

- Administer directly into the bloodstream.
- Use as ordered by your healthcare provider.
- You should be trained on how to do intravenous injections by your healthcare provider or hemophilia treatment center. Once trained, many patients with hemophilia A are able to inject this medicine by themselves or with the help of a family member.
- Your healthcare provider will tell you how much to use based on your weight, the severity of your hemophilia A, and where you are bleeding.
- You may need to have blood tests done after getting to be sure that your blood level of Factor VIII is high enough to clot your blood.
- Call your healthcare provider right away if your bleeding does not stop after taking this medicine.

What are the possible side effects of AFSTYLA?

- Allergic reactions may occur. Immediately stop treatment and call your healthcare provider right away if you get a rash or hives, itching, tightness of the chest or throat, difficulty breathing, light-headedness, dizziness, nausea, or decrease in blood pressure.
- Your body may form inhibitors to Factor VIII. An inhibitor is a part of the body's defense system. If you form inhibitors, it may stop this medicine from working properly. Your healthcare provider may need to test your blood for inhibitors from time to time.
- Common side effects are dizziness and allergic reactions.
- These are not the only side effects possible. Tell your healthcare provider about any side effect that bothers you or does not go away.

What else should I know about AFSTYLA?

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

Please see full prescribing information, including full FDA-approved patient labeling. For more information, visit www. AFSTYLA.com

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HEMAWARE
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Cover photography by Nilesh Bhange/Thinkstock

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hemaware.org/en-espanol

▶ **CÓMO PREPARAR A SU HIJO PARA UNA CIRUGÍA**
La planificación ayuda a aliviar inquietudes y aumentar la seguridad
hemaware.org/node/1681

▶ **A PONERSE ROJO**
La información y defensa son fundamentales en la misión de NHF
hemaware.org/node/1678

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online +

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ADYNOVATE
[Antihemophilic Factor (Recombinant), PEGylated]

\+ PROVEN PROPHYLAXIS

SIMPLE,* TWICE-WEEKLY DOSING SCHEDULE

= *moments* YOUR WAY

Proven results with ADYNOVATE

+ **Zero median ABR** for joint or spontaneous bleeding episodes with ADYNOVATE prophylaxis†[1]

* ADYNOVATE allows you to infuse on the same 2 days every week.[1]

† Joint: 0.0 (Q1: 0.0; Q3: 2.0) median vs on-demand 38.1 (Q1: 24.5; Q3: 44.6); 2.9 (SD 8.0) mean vs on-demand 34.7 (SD 15.1). Spontaneous: 0.0 (Q1: 0.0; Q3: 2.2) median vs on-demand 21.6 (Q1: 11.2; Q3: 33.2); 2.9 (SD 7.1) mean vs on-demand 26.0 (SD 19.6).[1,2]

The safety, efficacy, and PK of ADYNOVATE were evaluated in a multicenter, open-label, prospective, nonrandomized, 2-arm clinical study (N=137) that compared the efficacy of a twice-weekly prophylactic treatment regimen to on-demand treatment and determined hemostatic efficacy in the treatment of bleeding episodes.[1]

For patients 12 years and older with hemophilia A

To see if ADYNOVATE may be right for you, visit **www.ADYNOVATE.com**

ABR=annualized bleeding rate.

ADYNOVATE [Antihemophilic Factor (Recombinant), PEGylated] Important Information

Indication

ADYNOVATE is used on-demand to control bleeding in patients 12 years of age and older with hemophilia A. ADYNOVATE can reduce the number of bleeding episodes when used regularly (prophylaxis).

ADYNOVATE is not used to treat von Willebrand disease.

DETAILED IMPORTANT RISK INFORMATION

You should not use ADYNOVATE if you:
- Are allergic to mice or hamster protein
- Are allergic to any ingredients in ADYNOVATE or ADVATE [Antihemophilic Factor (Recombinant)]

Tell your healthcare provider if you are pregnant or breastfeeding because ADYNOVATE 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 ADYNOVATE 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 ADYNOVATE 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 ADYNOVATE. 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.

The common side effects of ADYNOVATE are headache and nausea. Tell your healthcare provider about any side effects that bother you or do not go away.

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 ADYNOVATE Important Facts.

References: 1. ADYNOVATE Prescribing Information. Westlake Village, CA: Baxalta US Inc.
2. Data on file. Baxalta Incorporated.

Shire

ADYNOVATE [Antihemophilic Factor (Recombinant), PEGylated]

Important facts about

ADYNOVATE [Antihemophilic Factor (Recombinant), PEGylated]

This leaflet summarizes important information about ADYNOVATE. Please read it carefully before using this medicine. This information does not take the place of talking with your healthcare provider, and it does not include all of the important information about ADYNOVATE. If you have any questions after reading this, ask your healthcare provider.

What is the most important information I need to know about ADYNOVATE?

Do not attempt to do an infusion to yourself unless you have been taught how by your healthcare provider or hemophilia center.

You must carefully follow your healthcare provider's instructions regarding the dose and schedule for infusing ADYNOVATE so that your treatment will work best for you.

What is ADYNOVATE?

ADYNOVATE is an injectable medicine used to replace clotting factor (factor VIII or antihemophilic factor) that is missing in people with hemophilia A (also called "classic" hemophilia). Hemophilia A is an inherited bleeding disorder that prevents blood from clotting normally.

ADYNOVATE is used on-demand to control bleeding in patients 12 years of age and older with hemophilia A. ADYNOVATE can reduce the number of bleeding episodes when used regularly (prophylaxis).

ADYNOVATE is not used to treat von Willebrand disease.

Who should not use ADYNOVATE?

You should not use ADYNOVATE if you:

- Are allergic to mice or hamster protein
- Are allergic to any ingredients in ADYNOVATE or ADVATE

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

How should I use ADYNOVATE?

ADYNOVATE is given directly into the bloodstream.

You may infuse ADYNOVATE at a hemophilia treatment center, at your healthcare provider's office or in your home. You should be trained on how to do infusions by your healthcare provider or hemophilia treatment center. Many people with hemophilia A learn to infuse their ADYNOVATE by themselves or with the help of a family member.

Your healthcare provider will tell you how much ADYNOVATE to use based on your individual weight, level of physical activity, the severity of your hemophilia A, and where you are bleeding.

Reconstituted product (after mixing dry product with wet diluent) must be used within 3 hours and cannot be stored or refrigerated. Discard any ADYNOVATE left in the vial at the end of your infusion as directed by your healthcare professional.

How should I use ADYNOVATE? (cont'd)

You may have to have blood tests done after getting ADYNOVATE to be sure that your blood level of factor VIII is high enough to clot your blood.

Call your healthcare provider right away if your bleeding does not stop after taking ADYNOVATE.

What should I tell my healthcare provider before I use ADYNOVATE?

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.
- Are breastfeeding. It is not known if ADYNOVATE passes into your milk and if it can harm your baby.
- Are pregnant or planning to become pregnant. It is not known if ADYNOVATE may harm your unborn baby.
- Have been told that you have inhibitors to factor VIII (because ADYNOVATE may not work for you).

What are the possible side effects of ADYNOVATE?

You can have an allergic reaction to ADYNOVATE.

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.

The common side effects of ADYNOVATE are headache and nausea. Tell your healthcare provider about any side effects that bother you or do not go away.

These are not all the possible side effects with ADYNOVATE. You can ask your healthcare provider for information that is written for healthcare professionals.

What else should I know about ADYNOVATE and Hemophilia A?

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 ADYNOVATE 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.

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

The risk information provided here is not comprehensive. To learn more, talk with your health care provider or pharmacist about ADYNOVATE. The FDA approved product labeling can be found at www.ADYNOVATE.com or 855-4-ADYNOVATE.

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.

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Issued 11/2015

15E001-ADY-US

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Groundbreaking Guideline

BY MENAKA PAI, BSC, MSC, MD, FRCPC

This issue features an in-depth look at the National Hemophilia Foundation (NHF)-McMaster Guideline on Care Models in Hemophilia (See "Well-grounded Guideline," page 16) , published in the journal *Haemophilia* and presented at NHF's 68th Annual Meeting in July in Orlando, Florida.

This guideline is a major achievement for NHF. It furthers its goal to find better treatments and cures for bleeding disorders through education, advocacy and research support. The Guideline on Care Models acknowledges that the healthcare landscape in the US is changing rapidly, as is the natural course of hemophilia. Now that people with hemophilia are living longer and living better, it is essential that evidence-based clinical practice guidelines are created to support patient-centered decision-making. These guidelines help ensure patients with hemophilia receive the right care, delivered in the right way.

The Guideline on Care Models is the first published clinical practice guideline in any field of medicine conceived of and sponsored by a patient organization. It also is unique in a few other respects.

All clinical practice guidelines must be built on a solid foundation of evidence, which can be a challenge in rare diseases like hemophilia, where there are relatively few published scientific papers. So the team of health researchers from McMaster University developed new methods to gather and develop evidence to support the guideline. These new methods, described in supporting papers in *Haemophilia*, can be used to bolster guideline development in other rare diseases.

The panel that made the final recommendations is also distinctive. Very often, panels consist exclusively of physicians. These physicians may have tremendous experience treating the target disease, but they may not be able to speak to all of the aspects of clinical care that are important to patients. By contrast, NHF and McMaster University aimed for both breadth and depth of expertise in assembling the panel. Panelists included not only physicians but also people with hemophilia, parents of people with hemophilia, individuals with other rare diseases, payers, researchers, nurses, physical therapists and genetic counselors. This group offered a host of different viewpoints, all of which were considered in developing the guideline.

The purpose of the Guideline on Care Models is to identify best practices in hemophilia care, and to discuss the range of care providers and services that are most important for people with hemophilia across the US. The hope of the panel, and the NHF-McMaster development team, is that the guideline will be an important resource for anyone affected by or providing care for this disease.

Menaka Pai, BSc, MSc, MD, FRCPC, is an associate professor in the Department of Medicine and an associate member of the Department of Pathology and Molecular Medicine at McMaster University in Hamilton, Canada. She was a member of the guideline panel.

The National Hemophilia Foundation is dedicated to finding better treatments and cures for inheritable bleeding disorders and to preventing the complications of these disorders through education, advocacy and research.

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All manuscript submissions should be typed double space, between 500 and 1,000 words in length and sent via e-mail to libby.hawkins@manifest.com. *HemAware* retains the right to edit submissions. The content of the article is the responsibility of the author(s) and must be original work that has not been, nor will be, published elsewhere. A copyright agreement attesting to this and transferring copyright to NHF is required.

Acceptance of advertising for products and services in *HemAware* in no way constitutes endorsement by the National Hemophilia Foundation.

ANTACIDS CAN CAUSE BLEEDING

After that pepperoni pizza that gave you heartburn, you may reach for relief in the form of an antacid. But be careful: Some antacids contain aspirin, which is generally taboo for people with bleeding disorders because of the increased risk of bleeding. The US Food and Drug Administration (FDA) released a safety announcement in June, warning consumers to read antacid labels, after receiving reports of serious bleeding in some people.

Antacids that contain aspirin include generics and trade names you may recognize, such as Alka-Seltzer Original and Bromo Seltzer.

According to the FDA, risk factors that increase the likelihood of a bleed in the stomach or gastrointestinal tract include:

- Being older than 60
- Having a history of stomach ulcers or bleeding problems
- Taking other medicines that contain nonsteroidal anti-inflammatories (NSAIDs), such as ibuprofen or naproxen

Source: fda.gov

BEFORE KINDERGARTEN: BEHAVIOR THERAPY FOR ADHD

All kids test their parents, but children with attention deficit hyperactivity disorder (ADHD) have even more challenging behaviors. The uncontrolled running, touching and yelling outbursts may have parents reaching for a prescription to tone down the behavior. But first, consider behavior therapy, says the US Centers for Disease Control and Prevention (CDC).

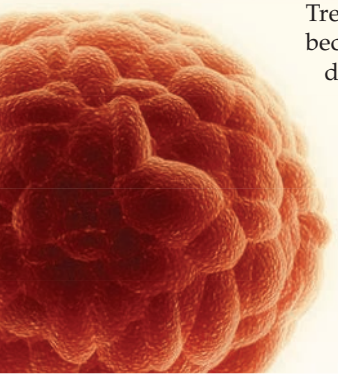
Along with the American Academy of Pediatrics, the CDC is urging healthcare providers to encourage parents of children with ADHD who are 4 to 5 years old to complete at least eight sessions of behavioral therapy training. "It has been shown to be as effective as medicine, but without the risk of side effects," says Anne Schuchat, MD, CDC principal deputy director.

Behavior therapy sessions teach parents how to become active listeners, help children describe emotions, reward positive behavior, overlook unwanted behavior and effectively use timeouts.

Studies have shown that such training helps kids improve their behavior, gain self-control and increase their self-esteem. Further, it helps improve communication between parent and child, and strengthens their bond.

For resources on behavior therapy: cdc.gov/ncbddd/adhd/behavior-therapy.html

Researchers Develop Cancer-Killing Antibodies



Treating cancer using chemotherapy and radiation can be effective, but it can also be destructive. That's because it often kills healthy cells. Researchers at Duke University may have found a solution: antibodies derived from human cells that kill cancer cells only. The results of the study were published May 5 in *Cell Reports* online.

The investigators, led by Edward Patz, Jr., MD, had noticed that tumors in certain patients with lung cancer were kept at bay. The protective mechanism was the presence of antibodies to the protein, called complement factor H (CFH), which prevents the immune system from mounting an attack.

Using patients' white blood cells to locate the antibodies, researchers cloned their genes and tested them. The antibodies killed tumor cells in lung, gastric and breast cancer cells in mice without harming healthy cells. "We believe we can modulate the immune response and let the body's own immune system take over to either kill the tumor or keep it from growing," Patz said in a press release.

Source: dukemedicine.org

Continues on page 11

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Now Approved for Hereditary Factor X Deficiency

Coagadex®

Coagulation Factor X (Human)

The first and only treatment specifically for hereditary factor X deficiency

- In clinical studies, COAGADEX was proven effective for on-demand treatment and surgical pocedures in patients with hereditary factor X deficiency
- COAGADEX is a high-purity factor X product with factor X content listed on every vial

Visit **www.coagadex.com** for ordering information

Please see the Brief Summary of Prescribing Information on accompanying page.

Indications for COAGADEX

COAGADEX, a plasma-derived blood coagulation factor X concentrate, is indicated in adults and children (aged 12 years and above) with hereditary factor X deficiency for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding in patients with mild hereditary factor X deficiency

Perioperative management of bleeding in major surgery in patients with moderate and severe hereditary factor X deficiency has not been studied.

Important Safety Information for COAGADEX

COAGADEX is contraindicated in patients with known hypersensitivity to any of the components of the product.

Allergic type hypersensitivity reactions, including anaphylaxis, are possible with COAGADEX. If symptoms occur, patients should discontinue use of the product immediately and contact their physician.

The formation of neutralizing antibodies (inhibitors) to factor X is a possible complication in the management of individuals with factor X deficiency. Carefully monitor patients taking Coagadex for the development of inhibitors by appropriate clinical observations and laboratory tests.

COAGADEX is made from human plasma and may contain infectious agents, e.g. viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. No cases of transmission of viral diseases, vCJD or CJD, have been associated with the use of COAGADEX.

In clinical studies, the most common adverse reactions (frequency ≥5% of subjects) with COAGADEX were infusion site erythema, infusion site pain, fatigue and back pain.

Please refer to the Coagadex Prescribing Information for full prescribing details.

REFERENCE

1. COAGADEX® (Coagulation Factor X, Human) Prescribing Information. Durham, NC: BPL Limited. 2015.

March 2016 US/X/0316/0004

bpl

Bio Products Laboratory

a commitment for life

For medical information queries, please call **1-866-398-0825** or email MedInfo@BPL-US.com

Coagadex HCP Brief Summary

The following is a brief summary only. See complete prescribing information on www.coagadex.com or request complete prescribing information by calling 1-866-398-0825.

INDICATIONS AND USAGE

COAGADEX, Coagulation Factor X (Human), is a plasma-derived human blood coagulation Factor indicated in adults and children (aged 12 years and above) with hereditary Factor X deficiency for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding in patients with mild hereditary Factor X deficiency.

Limitation of Use

Perioperative management of bleeding in major surgery in patients with moderate and severe hereditary Factor X deficiency has not been studied.

CONTRAINDICATIONS

COAGADEX is contraindicated in patients who have had life-threatening hypersensitivity reactions to COAGADEX or any of the components.

WARNINGS AND PRECAUTIONS

Hypersensitivity

Allergic type hypersensitivity reactions, including anaphylaxis, are possible. Early signs of hypersensitivity reactions including angioedema, infusion site inflammation (e.g. burning, stinging, erythema), chills, cough, dizziness, fever, flushing, generalized urticaria, headache, hives, hypotension, lethargy, musculoskeletal pains, nausea, pruritus, rash, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing. If hypersensitivity symptoms occur, discontinue use of the product immediately and administer appropriate emergency treatment.

COAGADEX contains traces of human proteins other than Factor X.

Neutralizing Antibodies

The formation of neutralizing antibodies (inhibitors) to Factor X may occur. Monitor all patients treated with COAGADEX for the development of inhibitors by appropriate clinical observations and laboratory tests. If expected Factor X activity levels are not attained, or if bleeding is not controlled with an expected dose, perform an assay that measures Factor X inhibitor concentration.

Transmissible Infectious Agents

Because COAGADEX is made from human blood, it may carry a risk of transmitting infectious agents, e.g. viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. There is also the possibility that unknown infectious agents may be present in the product. The risk that the product will transmit viruses has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and removing certain viruses during manufacture. Despite these measures, this product may still potentially transmit diseases.

All infections suspected by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare providers to BPL Inc. at 1-866-398-0825.

Monitoring and Laboratory Tests

- Monitor plasma Factor X activity by performing a validated test (e.g. one-stage clotting assay), to confirm that adequate Factor X levels have been achieved and maintained.
- Monitor for the development of Factor X inhibitors. Perform a Bethesda inhibitor assay if expected Factor X plasma levels are not attained, or if bleeding is not controlled with the expected dose of COAGADEX. Use Bethesda Units (BU) to report inhibitor levels.

ADVERSE REACTIONS

The most common adverse drug reactions (frequency ≥ 5% of subjects) observed in clinical trials were infusion site erythema, infusion site pain, fatigue, and back pain.

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 trial of another drug and may not reflect the rates observed in clinical practice.

During the clinical development of COAGADEX involving two multicenter, open-label, non-randomized clinical studies, 18 individual subjects with hereditary Factor X deficiency received at least one dose of COAGADEX.

Sixteen subjects aged 12 to 58 years with moderate to severe hereditary Factor X deficiency (basal FX:C < 5 IU/dL) received doses of COAGADEX for pharmacokinetic evaluation, on-demand treatment and control of bleeding episodes, and/or perioperative management of minor surgical or dental procedures. A total of 468 infusions were administered, including 242 for on-demand treatment and control of bleeding episodes, 6 for perioperative management and 31 for PK assessments. Spontaneous, traumatic and menorrhagic bleeding episodes were treated with a dose of 25 IU/kg for up to 2 years.

Two subjects aged 55 and 59 years with mild hereditary Factor X deficiency (basal FX:C 6 IU/dL and 8 IU/dL) received COAGADEX for perioperative management of four major surgical procedures. There were 40 exposure days to COAGADEX.

Immunogenicity

All subjects underwent Factor X inhibitor testing (inhibitor screen and Nijmegen-Bethesda assay) at baseline, end of study and at 3-monthly intervals in between. For subjects who underwent surgery, inhibitor testing was done pre-surgery and on discharge. All inhibitor tests were negative. Additionally, comparison of pharmacokinetic (PK) parameters at the repeat PK assessment with those at first dose did not suggest development of any inhibitors to Factor X.

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, it may be misleading to compare the incidence of antibodies to COAGADEX in the studies described above with the incidence of antibodies in other studies or to other products.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary: There are no data with COAGADEX use in pregnant women to inform on drug-associated risk. Animal reproduction studies have not been conducted using COAGADEX. It is not known whether COAGADEX can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. COAGADEX should be given to a pregnant woman only if clearly needed. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Lactation

Risk Summary: There is no information regarding the presence of COAGADEX in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COAGADEX and any potential adverse effects on the breast-fed infant from COAGADEX or from the underlying maternal condition.

Pediatric Use

Safety and effectiveness in patients under the age of 12 years have not been established.

Geriatric Use

Clinical studies of COAGADEX did not include any subjects aged 65 and over to determine whether they respond differently from younger subjects. Individualize dose selection for geriatric patients.

PATIENT COUNSELING INFORMATION

- Advise the patients to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
- Inform patients to immediately report the following early signs and symptoms of hypersensitivity reactions to their healthcare professional: angioedema, infusion site inflammation (e.g. burning, stinging, erythema), chills, cough, dizziness, fever, flushing, generalized urticaria, headache, hives, hypotension, lethargy, musculoskeletal pains, nausea, pruritus, rash, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing.
- Inform patients that the development of inhibitors to Factor X is a possible complication of treatment with COAGADEX. Advise the patients to contact their healthcare provider for further treatment and/or assessment if they experience a lack of clinical response to COAGADEX because this may be a manifestation of an inhibitor.
- Inform patients that COAGADEX is made from human plasma and may contain infectious agents that can cause diseases. While the risk that COAGADEX can transmit an infection has been reduced by screening plasma donors for prior exposure, testing donated plasma, and inactivating or removing certain viruses during manufacturing, patients should report any symptoms that concern them

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.

To report adverse events, or for additional information, call 1-866-398-0825.

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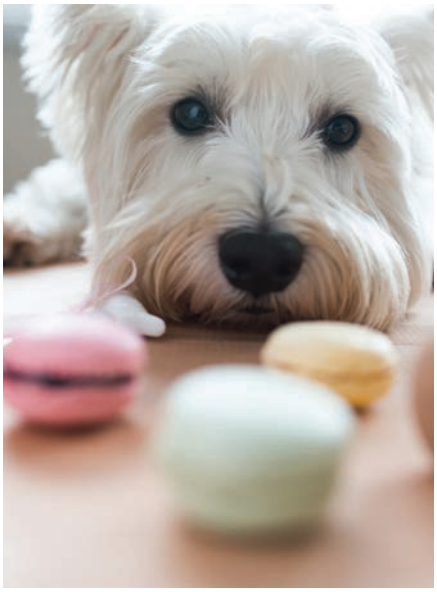


From Left: Indigo-stock/ThinkStock; Warayoo/ThinkStock

SUGAR-FREE PRODUCTS ARE DOGGONE

Many dogs are drawn to sweets, but a common ingredient in some sugarless products might kill them. Xylitol, a sugar substitute found in everything from nut butter to mouthwash and sugar-free gum, isn't metabolized the same way in canines as it is in humans. It can cause severe hypoglycemia (low blood sugar) within 60 minutes of your dog eating a xylitol-containing product.

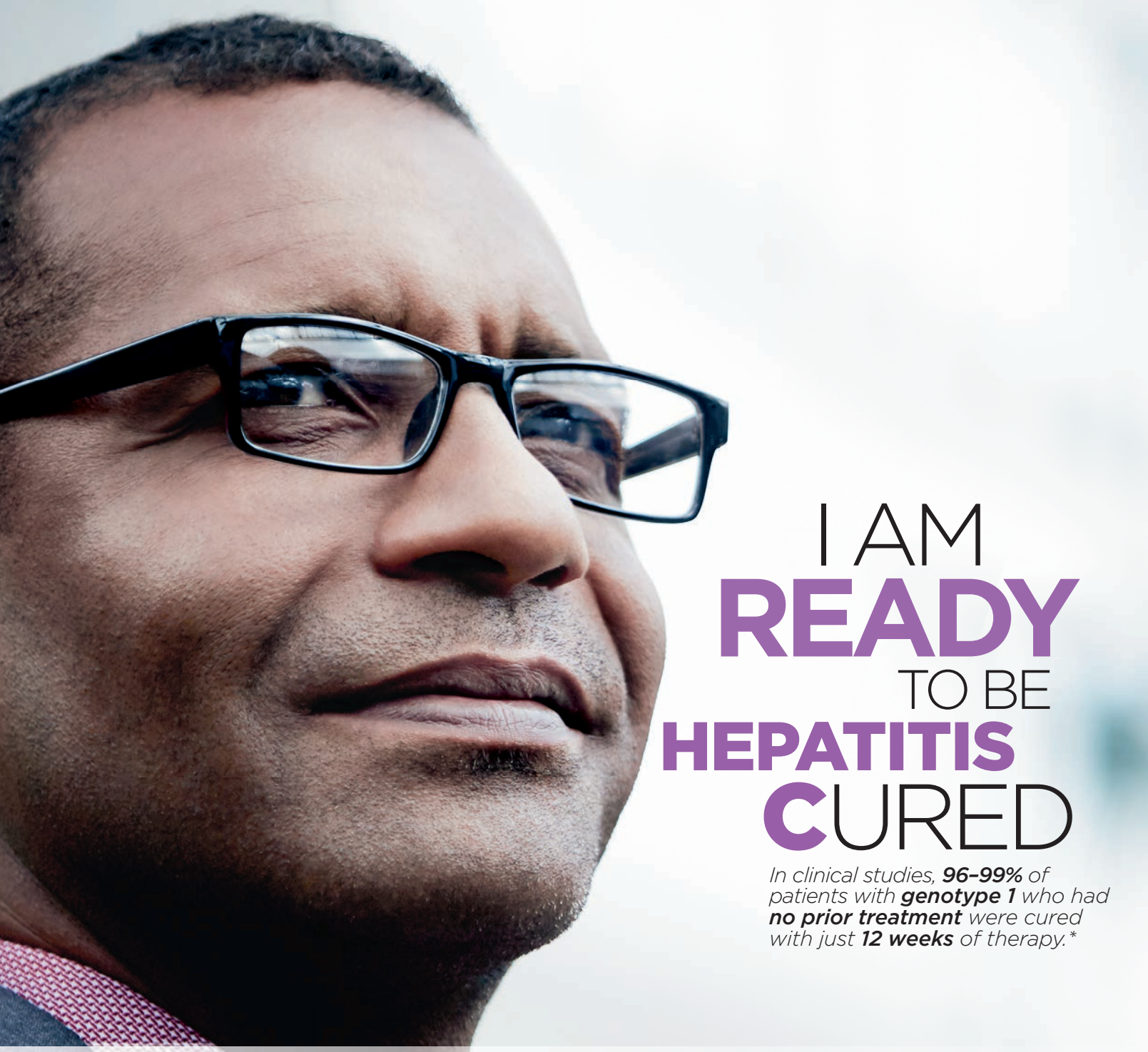
Products that may contain xylitol include:

- Chewing gum
- Breath mints
- Mouthwash
- Toothpaste
- Cough syrup
- Baked goods
- Chewable vitamins

The Center for Veterinary Medicine at the US Food and Drug Administration (FDA) encourages dog owners to keep xylitol-containing products away from their pets. Also, never use human toothpaste to brush your dog's teeth. Be careful if you sneak your dog's prescription pill into a dab of peanut butter—it may contain xylitol.

Source: fda.gov

Continues on page 15



I AM READY TO BE HEPATITIS CURED

*In clinical studies, **96–99%** of patients with **genotype 1** who had **no prior treatment** were cured with just **12 weeks** of therapy.**

* In a study of 865 patients with genotype 1 Hep C and no prior Hep C treatment, with or without advanced liver disease (cirrhosis), 99% (210 out of 213) of those who received HARVONI once daily for 12 weeks were cured. In a separate study of 647 patients with genotype 1 Hep C, with no prior Hep C treatment and without cirrhosis, 96% (208 out of 216) of those who received HARVONI once daily for 12 weeks were cured.

† In the study of 647 patients with genotype 1 Hep C, with no prior Hep C treatment and without cirrhosis, 97% (119 out of 123) of those with lower levels of the virus (less than 6 million IU/mL) who received HARVONI once daily for 8 weeks were cured.

These studies did not include patients with liver failure or those who have had a liver transplant.

‡ Based on prescription data for U.S. patients starting Hep C treatment with advanced treatment regimens (including direct-acting antiviral medicines) from 5/2011–12/2015.[1]

GILEAD

TODAY THERE'S HARVONI. A BREAKTHROUGH TREATMENT FOR HEPATITIS C.

Now, more people have been prescribed HARVONI to cure their Hep C than any other advanced treatment regimen.‡

HARVONI is a prescription medicine used with or without ribavirin to treat chronic (lasting a long time) hepatitis C (Hep C) genotype 1, 4, 5 or 6 infection. It is not known if HARVONI is safe and effective in children under 18 years of age.

HARVONI has been proven to **cure up to 99% of patients** with **genotype 1** (the most common type of hepatitis C) who've had **no prior Hep C treatment**.*

HARVONI transformed Hep C treatment as the first cure that's one pill, once a day for 12 weeks. And for certain patients with genotype 1, HARVONI has been shown to be highly effective in as little as 8 weeks of treatment.† Your Hep C Specialist will decide what treatment length is right for you.

Cure means the Hep C virus is not detected in the blood when measured three months after treatment is completed.

With HARVONI, there's **no interferon and no complicated regimens**.

So, if you don't want to live with the uncertainties of Hep C, now may be the time to talk to your Hep C Specialist about HARVONI.

IMPORTANT SAFETY INFORMATION

What should I tell my healthcare provider before taking HARVONI?

- If you have: liver problems other than hepatitis C infection, or have had a liver transplant; severe kidney problems or are on dialysis; HIV, or any other medical condition; or if you are pregnant or breastfeeding or plan to become pregnant or breastfeed. It is not known if HARVONI will harm your unborn baby or pass into your breast milk. If you take HARVONI with ribavirin, you should also read the ribavirin Medication Guide for important pregnancy-related information.
- **Tell your healthcare provider and pharmacist about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. HARVONI and certain other medicines may affect each other, or may cause side effects. Tell your healthcare provider if you take any medicines containing tenofovir disoproxil fumarate (ATRIPLA®, COMPLERA®, STRIBILD®, TRUVADA®, VIREAD®).

What are the possible side effects of HARVONI?

- HARVONI, when taken with amiodarone (Cordarone®, Nexterone®, Pacerone®), a medicine used to treat certain heart problems, may cause serious side effects, including slow heart rate, which in some cases has led to death or the need for a pacemaker. Get medical help right away if you take amiodarone with HARVONI and get any of the following symptoms: fainting or near-fainting, dizziness or lightheadedness, not feeling well, weakness, extreme tiredness, shortness of breath, chest pains, confusion, or memory problems.
- The most common side effects of HARVONI include tiredness, headache and weakness.

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.

Are you ready for HARVONI? Ask your Hep C Specialist if HARVONI is right for you and visit HARVONI.com or call 1-844-READY41.

Please see Important Facts about HARVONI on the following page.

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HARVONI®
ledipasvir/sofosbuvir
90 mg/400 mg tablets

(har-VOE-nee)

IMPORTANT FACTS

This is only a brief summary of important information about HARVONI and does not replace talking to your healthcare provider about your condition and your treatment.

ABOUT HARVONI

HARVONI is a prescription medicine used with or without ribavirin to treat chronic (lasting a long time) hepatitis C genotype 1, 4, 5 or 6 infection in adults. It is not known if HARVONI is safe and effective in children under 18 years of age.

POSSIBLE SIDE EFFECTS OF HARVONI

HARVONI, when taken with amiodarone (Cordarone®, Nexterone®, Pacerone®), a medicine used to treat certain heart problems, may cause serious side effects, including slow heart rate, which in some cases has led to death or the need for a pacemaker. Get medical help right away if you take amiodarone with HARVONI and get any of the following symptoms:

- fainting or near-fainting
- dizziness or lightheadedness
- not feeling well
- weakness
- extreme tiredness
- shortness of breath
- chest pains
- confusion
- memory problems

The most common side effects include tiredness, headache and weakness.

These are not all the possible side effects of HARVONI. Tell your healthcare provider if you have any new symptoms while taking HARVONI.

BEFORE TAKING HARVONI

Tell your healthcare provider if you have:

- Liver problems other than hepatitis C infection
- Had a liver transplant
- Severe kidney problems or you are on dialysis
- HIV infection
- Any other medical condition

Tell your healthcare provider about all the medicines you take:

- Keep a list that includes all prescription and over-the-counter medicines, vitamins, and herbal supplements, and show it to your healthcare provider.
- Including any medicines containing tenofovir disoproxil fumarate (ATRIPLA®, COMPLERA®, STRIBILD®, TRUVADA®, VIREAD®).
- If you take HARVONI with ribavirin, you should also read the ribavirin Medication Guide for important pregnancy-related information.

HARVONI and certain medicines may affect each other, or cause side effects.

GET MORE INFORMATION

- This is only a brief summary of important information about HARVONI. Talk to your healthcare provider or pharmacist to learn more.
- Go to HARVONI.com or call 1-844-READY41
- If you need help paying for your medicine call 1-855-7-MYPATH or go to HARVONI.com/support

¶Retail Pharmacy prescription data from IMS NPA New to Brand™ U.S. patient starts between 5/2011 and 12/2015.

GILEAD

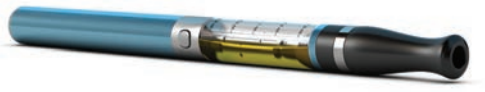
Continued from page 11

FDA to Regulate Hookahs and Electronic Cigarettes

Popularity is fanning the flame of electronic cigarettes, or e-cigarettes, among high schoolers. From 2011 to 2015, e-cigarette use among teenagers shot up from 1% to 16%. The use of hookahs, or water pipes shared in a communal setting, has also caught on among the younger set. But as of June 16, the US Food and Drug Administration (FDA) will begin to regulate these products, cigars and pipe tobacco.

Although e-cigarettes and hookahs may appear safer than cigarettes, they're not. Hookahs release tar, carbon monoxide, metals and cancer-causing agents into the air and your lungs. Because sessions can last 45 minutes, smokers inhale more nicotine than from a cigarette.

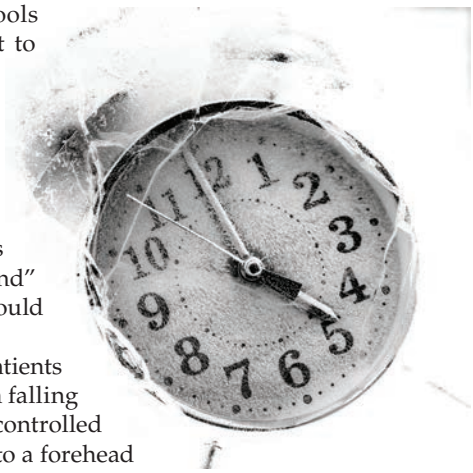
Source: fda.gov



From left: Olivier Le Moal/ThinkStock; Charles Taylor/Thinkstock

Insomnia? Just Chill Out

The latest breakthrough therapy to treat insomnia is not a pill, it's a pad. The Cerêve Sleep System, approved by the US Food and Drug Administration (FDA) in June, cools the forehead, allowing you to get to sleep more easily.



The prescription device was developed by Eric Nofzinger, MD, a board-certified sleep physician who studied brain scans of insomniacs. He found that the frontal cortex remained active in patients who described having a "racing mind" that wouldn't settle down so they could fall asleep.

In studies of their sleep systems, patients showed significant improvement in falling asleep when wearing the software-controlled device that cools and pumps fluid to a forehead pad that you wear all night. The device is expected to be available in 2017.

Source: fda.gov

Well-Grounded Guide

iStock

line

Evidence indicates comprehensive care model is ideal

By Amy Lynn Smith

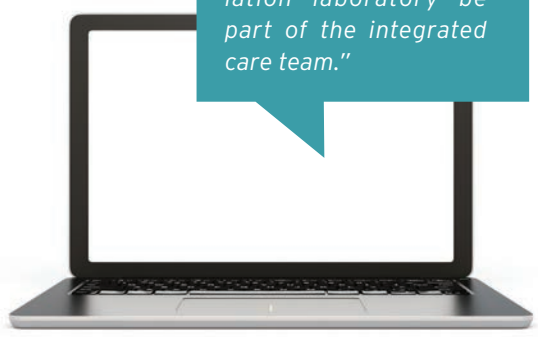
As people with bleeding disorders know, access to quality healthcare is essential to living well. But there hasn't been a widely accepted scientific resource to guide how that care should be delivered—until now. The National Hemophilia Foundation (NHF), in partnership with McMaster University in Hamilton, Ontario, Canada, has published a landmark evidence-based clinical practice guideline on care models for hemophilia management. Based on rigorous and innovative study methods, the guideline concludes that an integrated care model is ideal for people with hemophilia and other bleeding disorders.

Guideline at a Glance

The guideline was accepted July 8 and will be published on guidelines.gov, the website of the National Guideline Clearinghouse. Providers, healthcare system leaders, insurers and policy makers use this resource for evidence-based data when making decisions about the care they will provide and cover.

"The guideline panel suggests that the integrated care model be used over non-integrated care models for people with hemophilia, especially those at high risk for inhibitor development.

In addition, the panel suggests that a hematologist, a specialized hemophilia nurse, a physical therapist, a social worker, and round the-clock access to a specialized coagulation laboratory be part of the integrated care team."



Integrated care means all the services needed to effectively manage a health condition are provided by a multidisciplinary team like the staff at hemophilia treatment centers (HTCs). This may seem obvious to people with bleeding disorders who already rely on the comprehensive care provided at their HTCs. However, spelling out the conclusion in a clinical practice guideline is essential to supporting the goal for consistent, quality care for every person with a bleeding disorder.

"Patients should be going to facilities that deliver integrated care, and specialists who are delivering care should be providing it in an integrated fashion," says Mark Skinner, JD, a consultant who served on the panel to create the guideline. He has severe hemophilia A. "Having care delivered through an integrated care model makes a difference to patients. This data support that."

WHAT DOES IT MEAN FOR YOU?

The guideline is significant for a few reasons. First, it helps establish best practices. Second, it provides consumers solid backing when they go to bat for themselves or family members. This is particularly important when obtaining care outside an HTC. Common scenarios include emergencies and being cared for by community physicians between visits to an HTC. The guideline is a credible resource for care providers who don't treat bleeding disorders every day.

"The guideline is a tool for patients to use with insurers, employers and policy makers when advocating for access to specialized, high-quality care," says Ellen Riker, senior vice president at CRD Associates in Washington, DC, and a federal policy adviser to NHF. She served on the guideline panel for NHF. "We influence the environment that we live in. Evidence is often the best way to do it."

FROM PERCEPTION TO EVIDENCE

NHF has a long history of advocating for the needs of people with bleeding disorders. However, spearheading the development of an evidence-based clinical guideline was a new frontier. That's why the foundation partnered with McMaster University, which is known for its work in hematology and evidence-based medicine. Further, NHF provided the funding to support the creation of a multidisciplinary panel to do the work over a three-year period. Although many topics for the first guideline were discussed, the panel decided that care delivery was the place to start.

For many patients and medical professionals, it's common sense that integrated care provides better outcomes. Indeed, when everyone on the healthcare team works together coordinating care and sharing results, there's more consistency and attention to detail. Before creating the guideline, the data to back up this perception were sorely lacking.

One primary reason for this previous lack of evidence is the rarity of bleeding disorders. There simply aren't enough people to participate in the kind of large-scale studies usually conducted to make evidence-based recommendations. "Traditionally, you take a look at all of the published evidence and then you synthesize it. So we had to get creative here," says Menaka Pai, BSc, MSc, MD, FRCPC, one of the panelists. She is an associate professor

Continues on page 21

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Indications and Usage

NUWIQ® is a Recombinant Antihemophilic Factor [blood coagulation factor VIII (Factor VIII)] indicated in adults and children with Hemophilia A for on-demand treatment and control of bleeding episodes, perioperative management of bleeding, and for routine prophylaxis to reduce the frequency of bleeding episodes. NUWIQ is not indicated for the treatment of von Willebrand Disease.

Important Safety Information

NUWIQ is contraindicated in patients who have manifested life-threatening hypersensitivity reactions, including anaphylaxis, to the product or its components. The most frequently occurring adverse reactions (>0.5%) in clinical trials were paresthesia, headache, injection site inflammation, injection site pain, non-neutralizing anti-Factor VIII antibody formation, back pain, vertigo, and dry mouth. Development of Factor VIII neutralizing antibodies (inhibitors) may occur.

Please see adjacent page for Brief Summary of Prescribing Information.

www.nuwiqusa.com

References: 1. Sandberg H, et al. Thromb Res 2012; 130:808-817. **2.** Casademunt E, et al. Eur J Haematol 2012; 89:165-176. **3.** Kannicht C, et al. Thromb Res 2013; 131:78-88. **4.** Valentino LA, et al. Haemophilia 2014; 20:1-9.

Date of preparation: 9/2016. NUW-0109-CAD

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use NUWIQ safely and effectively. See full prescribing information for NUWIQ.

NUWIQ®, Antihemophilic Factor (Recombinant) Lyophilized Powder for Solution for Intravenous Injection
Initial U.S. Approval: 2015

INDICATIONS AND USAGE

NUWIQ is a recombinant antihemophilic factor [blood coagulation factor VIII (Factor VIII)] indicated in adults and children with Hemophilia A for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding
- Routine prophylaxis to reduce the frequency of bleeding episodes

NUWIQ is not indicated for the treatment of von Willebrand Disease.

DOSAGE AND ADMINISTRATION

For intravenous use after reconstitution

- Each vial of NUWIQ is labeled with the actual amount of Factor VIII potency in international units (IU).
- Determine dose using the following formula for adolescents and adults:

  Required IU = body weight (kg) x desired Factor VIII rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL)
- Dosing for routine prophylaxis:

Subjects	Dose (IU/kg)	Frequency of infusions
Adolescents [12-17 yrs] and adults	30-40	Every other day
Children [2-11 yrs]	30-50	Every other day or three times per week

- Frequency and duration of therapy depends on severity of the FVIII deficiency, location and extent of bleeding, and patient's clinical condition.

DOSAGE FORMS AND STRENGTHS

NUWIQ is available as a white sterile, non-pyrogenic, lyophilized powder for reconstitution in single-use vials containing nominally 250, 500, 1000 or 2000 IU Factor VIII potency.

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

- Hypersensitivity reactions, including anaphylaxis, are possible. Should symptoms occur, discontinue NUWIQ and administer appropriate treatment.
- Development of Factor VIII neutralizing antibodies (inhibitors) may occur. If expected plasma Factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform an assay that measures Factor VIII inhibitor concentration.
- Monitor all patients for Factor VIII activity and development of Factor VIII inhibitor antibodies.

ADVERSE REACTIONS

The most frequently occurring adverse reactions (>0.5%) in clinical trials were paresthesia, headache, injection site inflammation, injection site pain, non-neutralizing anti-Factor VIII antibody formation, back pain, vertigo, and dry mouth.

USE IN SPECIFIC POPULATIONS

Pediatric Use: Lower recovery, shorter half life and faster clearance in children aged 2 - ≤12 years. Higher doses and/or a more frequent dosing schedule for prophylactic treatment should be considered in pediatric patients aged 2 to 5 years.

PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Because hypersensitivity reactions are possible with NUWIQ, inform patients of the early signs of hypersensitivity reactions, including hives, generalized urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis. Advise patients to stop the injection if any of these symptoms arise and contact their physician, and seek prompt emergency treatment.

Advise patients to contact their physician or treatment center for further treatment and/or assessment if they experience a lack of clinical response to Factor VIII replacement therapy, as this may be a manifestation of an inhibitor.

Advise patients to consult with their healthcare provider prior to traveling. While traveling, patients should be advised to bring an adequate supply of NUWIQ based on their current treatment regimen.

To report SUSPECTED ADVERSE REACTIONS, contact Octapharma USA Inc. at 1-866-766-4860 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

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Continued from page 18

in the Department of Medicine and an associate member of the Department of Pathology and Molecular Medicine at McMaster University. She is also the transfusion medicine quality lead and consultant laboratory hematologist at the Hamilton Regional Laboratory Medicine Program.

Identifying the ways in which delivering care for hemophilia is similar to delivering care for other chronic diseases was one creative solution to gathering evidence. For example, ample data show that integrated care improves outcomes for people with diabetes. From that, the panel drew some indirect conclusions about how the care delivery model would apply to people with hemophilia.

A further innovative approach was the use of structured interviews with patients, caregivers and healthcare providers, asking about their experiences with care. In addition, the panel contacted experts in the field, seeking unpublished data from smaller studies or personal observations. This method helped the panel tap into what Pai calls "hidden pockets of knowledge" in the community.

UNCOMMON APPROACH YIELDS UNIQUE RESULTS

Another notable aspect of the panel was that it was made up of a cross section of the bleeding disorders community. "The fact that patients were sitting with the researchers and the clinicians, the payers and methodologists—all evaluating the evidence on equal footing—means there was a consensus among everyone involved, particularly patients," Skinner says.

In addition, this guideline wasn't led by a medical society, which is the case with most guidelines. "This is the first evidence-based guideline of its kind developed by an advocacy organization," says Marla Feinstein, NHF public policy analyst. She respresented NHF on the committee. "It really encompasses what we do as an organization, helping the community and all stakeholders understand access to care."

GROUNDED IN RIGOROUS RESEARCH

To make sure the document would be widely adopted in practice, the panel followed accepted principles for developing transparent, evidence-based guidelines. These principles are promoted by the Institute of Medicine, the National Guideline Clearinghouse and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. This last group sets parameters on how guidelines should be created. "The result is a guideline that is extremely rigorous and that the bleeding disorders community can really put their faith into," Pai says.

The use of exacting methodology is one reason the guideline was endorsed by three highly respected organizations: the American Society of Hematology (ASH), the International Society on Thrombosis and Haemostasis (ISTH) and the World Federation of Hemophilia (WFH). "ASH agreed that the final guideline is both methodologically rigorous and aligns with our values as an organization," says Nathan Connell, MD, MPH, a member of the Guideline Oversight Subcommittee and the Committee on Quality at ASH. He is a hematologist at Brigham and Women's Hospital in Boston, and a Harvard Medical School faculty member.

"Just because hemophilia and other bleeding disorders are considered rare does not mean that patients must settle for anything less than the best care."

What's more, the guideline validates the care model HTCs already use. "ASH members were excited to have the opportunity to participate in the guideline development process—to review and ultimately endorse it—because we feel there is value and benefit for the patient," Connell says. "Ultimately, what we're here to do is improve the care for the patients."

ACTIONABLE IMPROVEMENTS

Although HTCs already use an integrated care model, the way it's applied is inconsistent. "There are practice pattern variations around the country," Skinner says.

The panel carefully analyzed the evidence to come up with recommendations, including suggestions on how to implement them, with a goal of "harmonizing" care delivery across the US, says Pai. The ultimate objective was to create guidelines that improve treatment practices and patients' health, she adds.

"Some guidelines are scientifically sound but don't move the needle of care," Pai says. "This partnership, where you have an academic institution coming together with a highly active patient organization like NHF, helps us focus on that end goal of making a difference in the lives of people affected by the disease."

WHAT'S NEXT

This first guideline is only the beginning. NHF plans to conduct ongoing reviews to identify ways to improve the evidence base and make the guideline even more actionable for the bleeding disorders community. Additionally, the guideline will hopefully inspire HTCs and specialists to unify their data collection efforts, adds Pai. This may fuel additional research into the treatment of bleeding disorders.

"NHF is the standard-bearer in the rare disease community by saying, 'Yes, this is a rare disease, but we can still produce good guidelines and put out strong calls for research,'" Pai says. "Just because hemophilia and other bleeding disorders are considered rare does not mean that patients must settle for anything less than the best care.'" ●

Learn More

- For a summary of the guideline: http://onlinelibrary.wiley.com/doi/10.1111/hae.13008/abstract

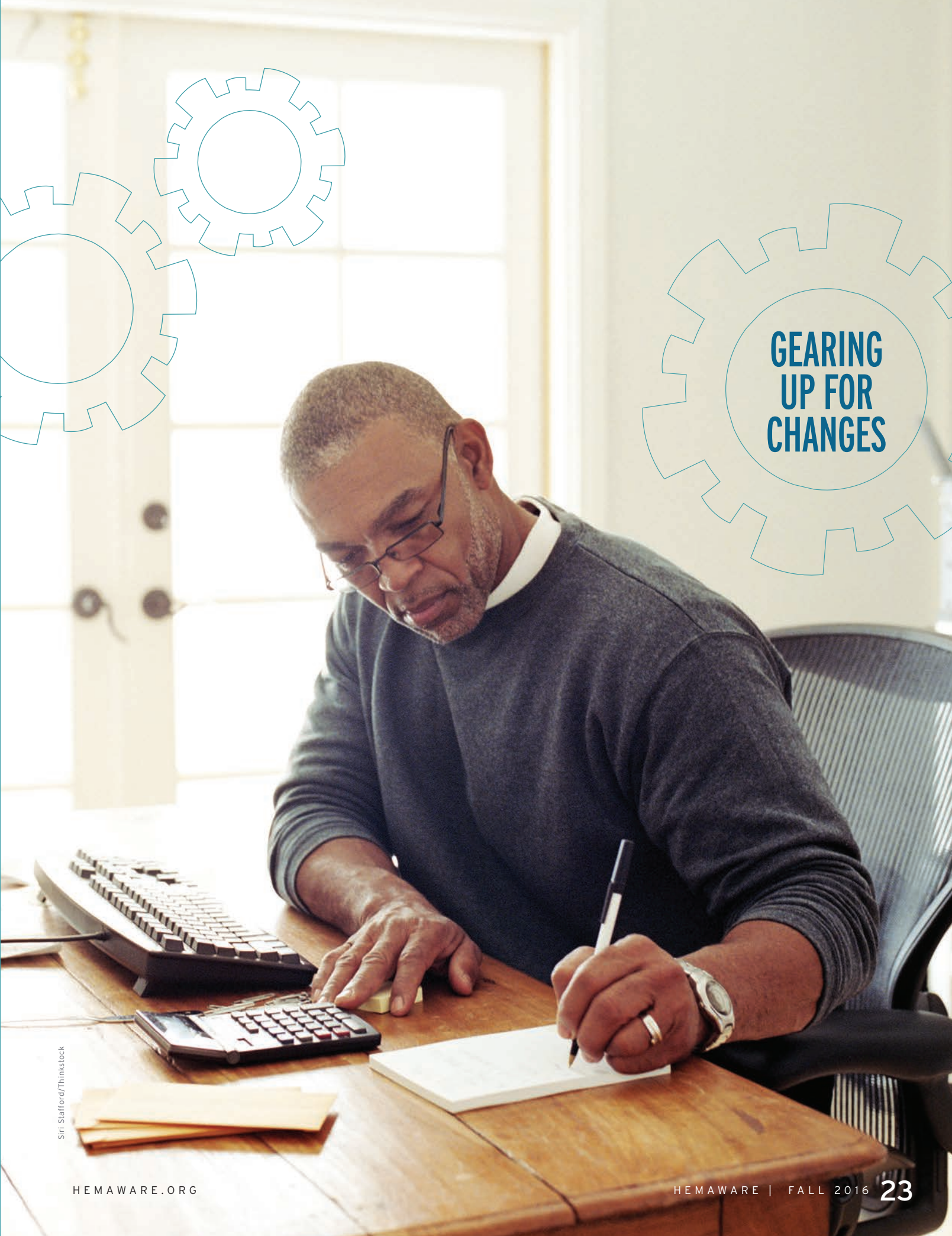
MINDING YOUR MEDICAID

By Kathryn Anne Stewart

More than a quarter of the bleeding disorders population in the US relies on Medicaid to pay health expenses. Medicaid, a government health program for low-income Americans, is a federal-state partnership. That means the federal government provides guidelines to follow, and states administer their individual programs.

Changes are afoot with this program, and they may create barriers to accessing clotting factor for some people. Here is what you must know and what the National Hemophilia Foundation (NHF) is doing to advocate for you.

GEARING UP FOR CHANGES



Siri Stafford/Thinkstock

UNDER THE MAGNIFYING GLASS

Just as all people have to be vigilant about their finances, state governments must find ways to stay within their budgets. "Unlike the federal government, local governments must have a balanced budget," explains Michelle Rice, NHF senior vice president for public policy and stakeholder relations.

Medicaid is a large part of every state's expenditures, comprising about one-quarter of total state budgets in 2013. That makes it a target for scrutiny. "It's important that patients understand these changes are not directed at one condition over another," says Marla Feinstein, NHF public policy analyst. "They're directed at controlling costs."

One option Medicaid programs don't have that private plans do is asking patients to pay more. "Under Medicaid, there are stricter rules about what a patient's out-of-pocket expenses can be," says Johanna Gray, senior vice president with CRD Associates in Washington, DC, and a federal policy adviser to NHF.

But Medicaid programs do have a few cost-cutting options. "They're either going to lower reimbursement, narrow networks or set up restrictive formularies," Rice says. "In some cases, they'll try to do all three."

Maxuser/ThinkStock

RESTRICTIVE FORMULARIES

Therapies to treat bleeding disorders are expensive, and costs are expected to rise. One obvious place for a state Medicaid plan to find savings is on its drug formulary, the list of all the drugs that it "covers," or pays for. If a drug is not on the list, the plan does not pay for it.

"Before, state Medicaid plans tended to include all types of clotting factor on their formularies," Gray says. Now, plans are being more restrictive about what's on the formulary. This is especially problematic for patients with bleeding disorders because they often respond better to one therapy over another. "It's a very unique disease. There's not a one-size-fits-all treatment or even a three-sizes-fit-all," Rice says.

A second concern is that formularies can be divided into preferred drug lists (PDLs). A PDL explains the level at which each drug is covered, typically organized by tiers. "Tier 1 means generic, tier 2 means preferred and tier 3 means nonpreferred," Rice explains. "As you go up the tiers, the amount of your copay increases." Some formularies include a tier 4, or specialty tier, in which patients pay a percentage of the drug's cost, called coinsurance. Because drugs to treat bleeding disorders are pricey, coinsurance amounts on them can be astronomical. NHF has been largely successful at keeping clotting factor drugs out of specialty tiers, Feinstein says.

In some Medicaid plans, the difference between tiers isn't monetary, but rather the type of approval you need. "You may have to get a prior authorization more often, or you may need a more detailed prior authorization," Rice says. "Some of them put more hurdles in place to access one of the newer, extended half-life drugs." Drugs with a longer half-life allow some patients to infuse less often.

The structure of a PDL encourages patients to opt for drugs from the lower tiers, ideally the tier 1, generic medications. "For most drugs, that's fine because there are generics available. But there are no generic clotting factor products," says Feinstein. In the past, there were fewer distinctions made between preferred (tier 2) and nonpreferred (tier 3) drugs for bleeding disorders because there were simply

Continues on page 27

NHF HAS BEEN LARGELY SUCCESSFUL AT KEEPING CLOTTING FACTOR DRUGS OUT OF SPECIALTY TIERS

Living with von Willebrand disease is complicated. Your treatment doesn't have to be.

wilate®

von Willebrand Factor/Coagulation Factor VIII Complex (Human)

If you have von Willebrand disease (VWD), you know that sometimes things can be very complicated.

WILATE helps to simplify VWD treatment with a natural 1:1 balance of VWF and FVIII that helps restore and maintain primary and secondary hemostasis for consistent and reliable control of bleeding.[1,2] And this 1:1 balance of factors in WILATE also means simple, straightforward dosing and very predictable measurements of factor activity, even after repeated infusions.[1,2]

wilate® The Simple Solution to a Complicated Disease.

Indications and Usage

WILATE is a von Willebrand Factor/Coagulation Factor VIII Complex (Human) indicated in children and adults with von Willebrand disease for on-demand treatment and control of bleeding episodes, and for perioperative management of bleeding.

WILATE is not indicated for the treatment of hemophilia A.

Important Safety Information

WILATE is contraindicated in patients with known hypersensitivity reactions, including anaphylactic or severe systemic reactions, to human plasma-derived products, any ingredient in the formulation, or components of the container.

WILATE is made from human plasma and carries the risk of transmitting infectious agents.

Please see adjacent page for Brief Summary of Prescribing Information.

www.wilateusa.com

References: 1. WILATE Full prescribing information. Hoboken, NJ: Octapharma; 2015. **2.** Berntorp et al. Haemophilia. 2009; 15:122-130.

Date of preparation: 9/2016. WIL-0111-CAD

octapharma®
For the safe and optimal use of human proteins

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use WILATE safely and effectively. See full prescribing information for WILATE.

WILATE, von Willebrand Factor/Coagulation Factor VIII Complex (Human) Lyophilized Powder for Solution for Intravenous Injection Initial U.S. Approval: 2009

RECENT MAJOR CHANGES

Indications and Usage 8/2015

INDICATIONS AND USAGE

WILATE is indicated in children and adults with von Willebrand disease for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding

WILATE is not indicated for treatment of hemophilia A

DOSAGE AND ADMINISTRATION

For Intravenous Use Only

- Use the following formula to determine required dosage:
  Required IU = body weight (BW) in kg x desired VWF:RCo rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL)
- Adjust dosage and duration of the substitution therapy depending on the severity of the VWD, on the location and extent of the bleeding, and on the patient's clinical condition
- Dosing recommendations:

Type of Hemorrhages/Surgery	Loading Dosage (IU VWF:RCo/ kg BW)	Maintenance Dosage (IU VWF:RCo/ kg BW)	Therapeutic Goal
Minor Hemorrhages	20-40 IU/kg	20-30 IU/kg every 12-24 hours	VWF:RCo and FVIII activity trough levels of >30%
Major Hemorrhages	40-60 IU/kg	20-40 IU/kg every 12-24 hours	VWF:RCo and FVIII activity trough levels of >50%
Minor Surgeries (including tooth extractions)	30-60 IU/kg	15-30 IU/kg or half the loading dose every 12-24 hours for up to 3 days	VWF:RCo peak level of 50% after loading dose and trough levels of >30% during maintenance doses
Major Surgeries	40-60 IU/kg	20-40 IU/kg or half the loading dose every 12-24 hours for up to 6 days or more	VWF:RCo peak level of 100% after loading dose and trough levels of >50% during maintenance doses

In order to decrease the risk of perioperative thrombosis, FVIII activity levels should not exceed 250%.

DOSAGE FORMS AND STRENGTHS

WILATE is available as a sterile, lyophilized powder for reconstitution for intravenous injection, provided in the following nominal strengths per single-use vial:

- 500 IU VWF:RCo and 500 IU FVIII activities in 5 mL
- 1000 IU VWF:RCo and 1000 IU FVIII activities in 10 mL

CONTRAINDICATIONS

Do not use in patients with known hypersensitivity reactions, including anaphylactic or severe systemic reaction, to human plasma-derived products, any ingredient in the formulation, or components of the container.

WARNINGS AND PRECAUTIONS

- Anaphylaxis and severe hypersensitivity reactions are possible.
- Thromboembolic events may occur. Monitor plasma levels of FVIII activity.
- Development of neutralizing antibodies to FVIII and to VWF, especially in VWD type 3 patients, may occur.
- WILATE is made from human plasma and carries the risk of transmitting infectious agents.

ADVERSE REACTIONS

The most common adverse reactions (≥1%) in clinical studies on VWD were hypersensitivity reactions, urticaria, and dizziness.

USE IN SPECIFIC POPULATIONS

Pregnancy: no human or animal data. Use only if clearly needed.

Lactation: There is no information regarding the presence of WILATE in human milk, the effect on the breastfed infant, and the effects on milk production.

Pediatric Use: No dose adjustment is needed for pediatric patients as administered dosages were similar to those used in the adult population.

Geriatric Use: Although some of the subjects who participated in the WILATE studies were over 65 years of age, the number of subjects was inadequate to allow subgroup analysis to support recommendations in the geriatric population.

PATIENT COUNSELING INFORMATION

- Advise the patients to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
- Inform patients of the early signs of hypersensitivity reactions including hives, generalized urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis. If allergic symptoms occur, advise patients to discontinue the administration immediately and contact their physician to administer appropriate emergency treatment.
- Inform patients that undergoing multiple treatments with WILATE may increase the risk of thrombotic events thereby requiring frequent monitoring of plasma VWF:RCo and FVIII activities.
- Inform patients that there is a potential of developing inhibitors to VWF, leading to an inadequate clinical response. Thus, if the expected VWF activity plasma levels are not attained, or if bleeding is not controlled with an adequate dose or repeated dosing, contact the treating physician.
- Inform patients that despite procedures for screening donors and plasma as well as those for inactivation or removal of infectious agents, the possibility of transmitting infective agents with plasma-derived products cannot be totally excluded.

To report SUSPECTED ADVERSE REACTIONS, contact Octapharma USA Inc. at 1-866-766-4860 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

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Revised: August 2015

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Continued from page 24
fewer drugs around. "Now, with the availability of more drugs and many more in the pipeline, PDLs are the only way for insurance companies to control costs," Rice says.

NHF's position:
NHF maintains that all FDA-approved therapies to treat hemophilia, von Willebrand disease and related bleeding disorders should be included on a health plan formulary, Rice says. Cost should not be the sole determining factor in where a drug is placed within the formulary. Clinical outcomes and patient need should be considered. If drugs are classified among preferred, nonpreferred and nonformulary tiers, there should be a clear, direct, timely process (a medically necessary exception provision) for the patient and his or her physician to follow to get the patient the needed drug. That process should not include the requirement that a patient first "fail" on another drug.

RESTRICTIVE PROVIDER NETWORKS

To control costs, some plans restrict their provider networks, particularly their pharmacy networks. In essence, your choice of pharmacies is limited to the few that carry factor and are also in your insurance plan's network. Gray notes that the number of pharmacies carrying clotting factor is already small. "We're living in a world where everything is getting narrowed," she says.

NHF's position:
There should be more than one qualified specialty pharmacy provider in a network. Preferably, there should be a specialty pharmacy option and one 340B option.

POTENTIAL CHANGES TO REIMBURSEMENT

In the next year, states will change the way they reimburse for drugs. The Centers for Medicare & Medicaid Services (CMS) announced a rule in January regarding reimbursement for retail pharmacy outpatient drugs (anything not considered a specialty drug). "The federal government is telling states that they need to reimburse based on what the pharmacy providers spent—their acquisition cost—plus a dispensing fee," Gray explains. "States have flexibility in setting the dispensing fee." They have until April 2017 to decide how they'll change their policies to comply with the new rule. Currently, states are determining what is a reasonable approach for clotting factor. "We are being hypervigilant with respect to these changes so they don't affect patients' access," says Feinstein.

NHF's position:
NHF does not suggest or recommend a specific drug price. Instead, reimbursement should be reasonable and adequate so as not to impede patient access.

WHAT YOU CAN DO

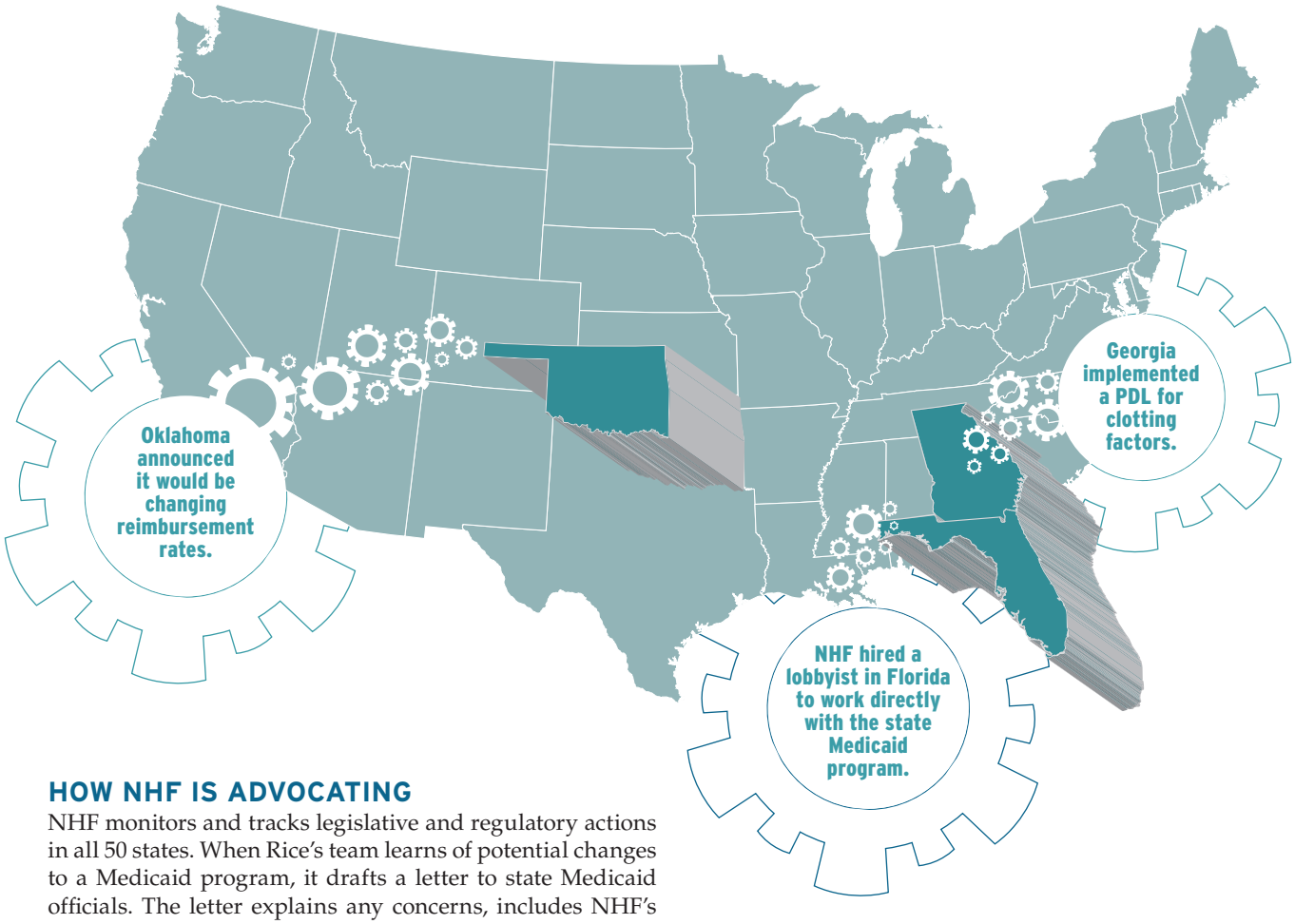
Most policy changes may seem out of your control, but here are some steps you can take to have a say:

> When choosing a health plan, do your research. "Read the policy. Ask for a copy of the drug formulary list. Ask if they have a separate formulary list for specialty pharmacy," says Michelle Rice, NHF senior vice president for public policy and stakeholder relations. "If you don't see your preferred drug on either the formulary or a specialty drug list, then call and find out if it's covered under major medical before you choose a plan." Almost all plans cover clotting factor, but you must know what steps you need to take to get it.

> Read and respond to your mail. "If anything comes to you from the state Medicaid program, open it and read it," Rice says. It may be a notification of an upcoming change. "You have some responsibility for then following those rules." Pharmacy providers and medical providers may also follow up on issues or request information from you through the mail.

> Remain vigilant. "These changes and how they affect an individual or a family or a caregiver are very specific," says Marla Feinstein, NHF public policy analyst. One alteration to a plan's policy may not affect you, but another might. If you see changes, Feinstein suggests asking follow-up questions such as: Why is this happening? Should I be concerned? How could this change my current care?

> Engage with the bleeding disorders support network. If you notice any access issues with your care, contact your chapter, NHF and your hemophilia treatment center. "There are resources to help people solve individual problems," says Johanna Gray, senior vice president with CRD Associates in Washington, DC, and a federal policy adviser to NHF. Plus, these organizations can identify larger trends that can prompt action. "That's what we can take to states, or we can take to Congress or we can take to CMS," Gray says. "But we need to hear from people to know that."



HOW NHF IS ADVOCATING

NHF monitors and tracks legislative and regulatory actions in all 50 states. When Rice's team learns of potential changes to a Medicaid program, it drafts a letter to state Medicaid officials. The letter explains any concerns, includes NHF's pertinent position statements and requests a phone conversation or in-person meeting.

NHF often involves other stakeholders in the process. "We will typically reach out to the chapter in that area and ask it to sign the letter with us," Rice says. NHF may invite a representative from the chapter to join in-person meetings with representatives from the Medicaid plans. Chapters and hemophilia treatment centers (HTCs) can help coach patients and physicians who are willing to share their powerful stories. When the changes under consideration have a detrimental impact, a local legislator may be involved as well.

During meetings, NHF provides education about bleeding disorders and strategies that have been effective in managing costs. "Keeping people with bleeding disorders healthy is the best strategy," Gray explains. For example, access to HTCs and clotting factor therapies without delay save costs in the long run, she adds.

ADVOCACY IN THREE SAMPLE STATES

For years, Medicaid patients in **Florida** were subject to a very restricted network for pharmacy providers. When the agency started the bidding process for new providers, NHF took action. "We hired a lobbyist in that state to work directly with the state Medicaid program to share our concerns about the size of the network and the contract requirements," Rice says. "We felt that very few people could even meet their requirements to apply to provide factor." The lobbying work was successful, and NHF's suggested alterations were made.

The Medicaid program in **Georgia** implemented a PDL for clotting factors, significantly reducing the number of drugs in the preferred category. "We explained what our concerns were, and they agreed to grandfather everybody who was currently on a product," Rice says. Georgia also created a very clear process by which a patient can access a nonpreferred drug.

Oklahoma announced it would be changing reimbursement rates, creating a PDL and establishing requirements that pharmacies had to meet to be an authorized Medicaid pharmacy. Officials clearly explained how to access therapies from the various tiers and what documentation would be necessary. "While it was a lot more rules than were in place before, we felt the treatment center was comfortable with what was going to be required," Rice says. She and her team ultimately wrote a letter commending the state for being proactive. "We want to make sure they know that we are supportive," Rice says.

Healthcare expenses are a big part of life when you have a bleeding disorder. As an informed consumer, understand your benefits and know your options. Meanwhile NHF will continue staying ahead of policy shifts to make your personal advocacy efforts a little easier. ●

Learn More

- Visit NHF's State Priorities page for more about NHF's priorities and perspective on health policy: hemophilia.org/Advocacy-Healthcare-Coverage/Advocacy-Priorities/State-Priorities
- Learn more Medicaid basics: kff.org/Medicaid

Jen's son, **Donovan**, lives with hemophilia A with inhibitors.

Jasmine lives with Glanzmann's thrombasthenia.

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We know you're on to the next great thing in your life. That's why NovoSecure™ was created. It's a new support program designed with your needs in mind. NovoSecure™ provides:

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Matthew lives with hemophilia A.

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Through WFH's Twinning Program, (back row, left to right) NHF CEO Val D. Bias, HFN president/founder Megan Adediran and NHF VP for Research and Medical Information Neil Frick, MS, have worked together to improve lives in Nigeria.

WFH's TWINNING PROGRAM BUILDS LASTING RELATIONSHIPS

POWER IN PARTNERSHIP

By Leslie Quander Wooldridge | Photo Illustrations by Gluekit

Megan Adediran didn't understand what was happening. After her son was born, he bled for five days after circumcision. A transfusion of whole blood from her husband finally stopped the hemorrhaging. It would be more than a year and three blood transfusions before Adediran's firstborn would be diagnosed with hemophilia.

Photos Courtesy of Megan Adediran

Megan Adediran (pictured above, seated in center) established the Haemophilia Foundation of Nigeria in 2005.

Medical staff did not expect the baby boy to live past age 3. "Hemophilia was like a death sentence," Adediran recalls from her home in Kaduna, about two hours from Nigeria's capital city of Abuja. There was no infrastructure on the ground to care for the few children and adults who were actually diagnosed. And medications and supplies to prevent and treat bleeds were severely lacking. "When your child is playing and you're not sure if he's going to fall to the ground and bleed in the brain and die, you are living in fear," Adediran says.

As she cared for her son past his third birthday and thought of the 13 other male relatives who had died from hemophilia-related complications, Adediran decided she needed to do something. In 2005, she established the Haemophilia Foundation of Nigeria (HFN) and registered it as a nongovernmental organization. Adediran is the organization's founder and president.

At first, Adediran's goal was simple. "I've always said I wanted to give my son a life." Now the mother of two boys with severe hemophilia A—Timothy, age 20, and Isaac, age 8—she also wanted to give hope to other people in Nigeria with bleeding disorders. To date, only an estimated 268 people there have been officially diagnosed with hemophilia. That leaves thousands potentially vulnerable to complications and even death from a bleeding disorder they may not know they have.

In 2013, HFN partnered with another World Federation of Hemophilia (WFH) member organization, the National Hemophilia Foundation (NHF), to significantly accelerate Adediran's goals.

Continues on page 40

THE WORLD FEDERATION OF HEMOPHILIA TWINNING PROGRAM PARTNERS EMERGING AND ESTABLISHED HEMOPHILIA PATIENT GROUPS TO SHARE KNOWLEDGE IN AREAS SUCH AS PATIENT EDUCATION, OUTREACH, FUNDRAISING AND ALL OTHER ASPECTS OF OPERATING A SUCCESSFUL HEMOPHILIA PATIENT SOCIETY.

Photo Courtesy of Megan Adediran

KOVALTRY®

EXPLORE WHAT'S POSSIBLE

KOVALTRY® is:

- **An unmodified recombinant Factor VIII offering the potential for as few as 2 infusions per week[1]**
- **Designed to closely match your body's natural Factor VIII[1]**
- **Based on a primary protein structure with more than 20 years of experience[1]**

KOVALTRY® Dosing: The recommended dose for routine prophylaxis in adults and adolescents is 20 to 40 IU of KOVALTRY® per kg of body weight 2x/week or 3x/week. The recommended dose for routine prophylaxis in children 12 years old and younger is 25 to 50 IU of KOVALTRY® per kg of body weight 2x/week, 3x/week, or every other day according to individual requirements.[1]

INDICATIONS

- KOVALTRY® is a medicine used to replace clotting factor (Factor VIII or antihemophilic factor) that is missing in people with hemophilia A.
- KOVALTRY® is used to treat and control bleeding in adults and children with hemophilia A. KOVALTRY® can reduce the number of bleeding episodes in adults and children with hemophilia A when used regularly (prophylaxis). Your healthcare provider may give you KOVALTRY® when you have surgery.
- KOVALTRY® is not used to treat von Willebrand Disease.

SELECTED IMPORTANT SAFETY INFORMATION

- You should not use KOVALTRY® if you are allergic to rodents (like mice and hamsters) or any ingredients in KOVALTRY®.

Please see continued Selected Important Safety Information on following pages. For additional important risk and use information, please see brief summary on following pages.

Kovaltry®

Antihemophilic Factor (Recombinant)

EXPLORE OUR COMMITMENT

Features designed to meet your needs

BAYER access solutions

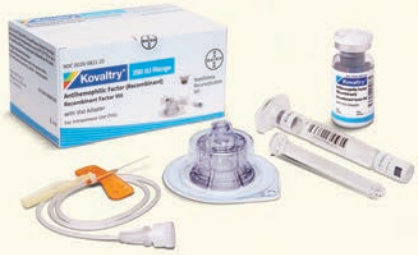
Don't let insurance or financial challenges get between you and your treatment*

- Trial Program at no cost to you
- Assistance during gaps in insurance coverage
- Co-pay support
- Patient support programs
- Live Helpline Support—**call 1-800-288-8374**
  8:00 AM-8:00 PM (ET) Monday-Friday

*Some restrictions apply. Please visit www.KOVALTRY.com or call 1-800-288-8374 for more information about the restrictions.

Vial Adapter reconstitution system[1]

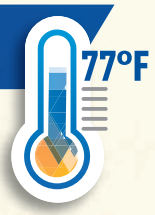
Needleless reconstitution system, including 2.5 mL or 5.0 mL prefilled diluent syringe and 25-gauge butterfly needle



Available in a wide range of vial sizes[1]

Reconstitution with 5 commonly needed vial sizes

Store at room temperature (up to 77°F) for up to 1 year*



*Store **KOVALTRY®** at 36°F to 46°F for up to 30 months from the date of manufacture. Do not freeze. Within this period, **KOVALTRY®** may be stored for a period of up to 12 months at temperatures up to 77°F. The starting date of room-temperature storage should be clearly recorded on the unopened product carton. Once stored at room temperature, the product must not be returned to the refrigerator. The shelf life then expires after the storage at room temperature (up to 12 months), or the expiration on the product vial, whichever is earlier. Do not use **KOVALTRY®** after the expiration date indicated on the vial and protect **KOVALTRY®** from extreme exposure to light.[1]

Please see full Prescribing Information for complete storage and handling instructions.

SELECTED IMPORTANT SAFETY INFORMATION

- Tell your healthcare provider if you have heart disease or are at risk for heart disease.
- The common side effects of KOVALTRY® are headache, fever, and itchy rash.
- Allergic reactions may occur with KOVALTRY®. Call your healthcare provider right away and stop treatment if you get tightness of the chest or throat, dizziness, decrease in blood pressure, and nausea.

EXPLORE SCIENCE THAT'S FOCUSED ON YOUR NEEDS

KOVALTRY® is manufactured using state-of-the-art technology

Heat Shock Protein 70 (HSP70), a chaperone protein, is used to improve proper folding of the Factor VIII protein[1]

No human- or animal-derived raw materials are added in the cell culture, purification, or formulation processes[1]

Passes through a microscopic filter (20 nm) to **remove viruses**[1]

KOVALTRY®

Unmodified, full length rFVIII product designed to closely match your body's natural Factor VIII[1]

nm=nanometer.
rFVIII=recombinant factor VIII.

SELECTED IMPORTANT SAFETY INFORMATION

- Your body can also make antibodies, called "inhibitors," against KOVALTRY®, which may stop KOVALTRY® 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.

Please see continued Selected Important Safety Information on following page. For additional important risk and use information, please see brief summary on following pages.

Kovaltry®
Antihemophilic Factor (Recombinant)

EXPLORE THE POSSIBILITIES WITH KOVALTRY®

LEOPOLD I studied the effectiveness and safety of KOVALTRY® in adolescents and adults (aged 12 to 65 years)[1]

Doctors chose **2x/week** or **3x/week** dosing based on each person's needs

PEOPLE IN THE STUDY[2]	ASSIGNED DOSING[2]	ABR RESULTS[1]
Group 1 (18 people) generally began the study with fewer bleeds and a lower percentage of target joints	2x/week	1 median ABR
Group 2 (44 people) generally began the study with more bleeds and a higher percentage of target joints	3x/week	2 median ABR

ABR=annual bleed rate—the number of bleeds in a year.
Median=the middle value of a set of numbers, placed in numerical order.

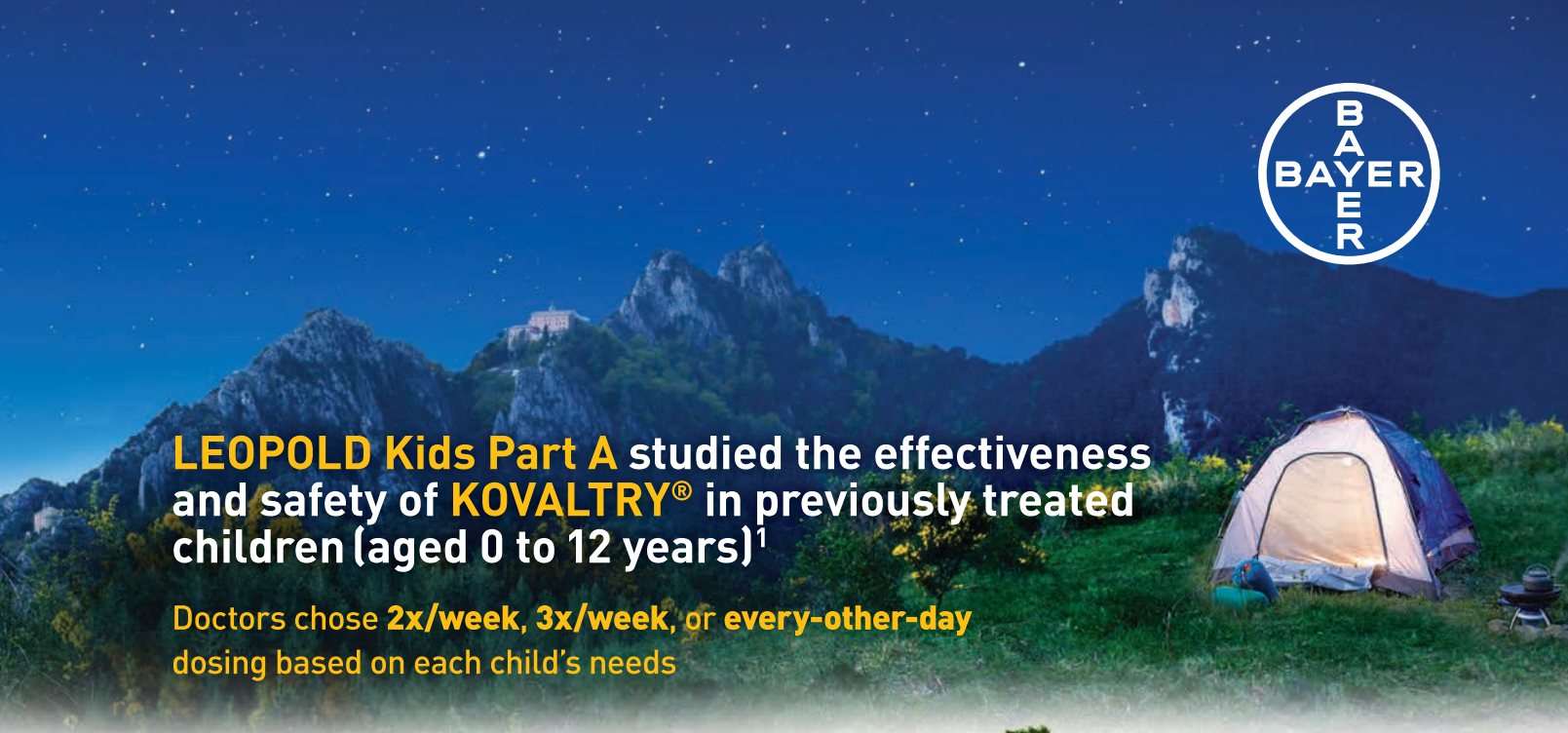
In the completed trial of 62 previously treated people, there were **0** inhibitors after one year on **KOVALTRY®**.[1]

- People with a history of inhibitors were not included in the trial. People with hemophilia A may develop inhibitors to rFVIII[1]

LEOPOLD I studied the effectiveness and safety of **KOVALTRY®** in 62 previously treated people with severe hemophilia, aged 12 to 65 years. For 1 year, doctors studied the ABR of these people. Dosing chosen for each person aligned with their individual characteristics—either 2x/week prophylaxis (18 people) or 3x/week prophylaxis (44 people).[1]

SELECTED IMPORTANT SAFETY INFORMATION

- Tell your healthcare provider about any side effect that bothers you or that does not go away.
- Call your healthcare provider right away if bleeding is not controlled after using KOVALTRY®.



LEOPOLD Kids Part A studied the effectiveness and safety of KOVALTRY® in previously treated children (aged 0 to 12 years)[1]

Doctors chose **2x/week**, **3x/week**, or **every-other-day** dosing based on each child's needs

Within 48 hours of each infusion, children in the study experienced a **median ABR** of

+

Throughout the entire study period, children experienced a **median ABR** of

In the completed trial of 51 previously treated children, there were **0** inhibitors after 6 months on **KOVALTRY®**.[1]

- Children with a history of inhibitors and those new to treatment were not included in the trial. Children with hemophilia A may develop inhibitors to rFVIII[1]

In an ongoing study, one 13-year-old previously treated child tested positive for a low-titer inhibitor. His ABR was 0 and no change in treatment was required.[1]

LEOPOLD Kids Part A studied the effectiveness and safety of **KOVALTRY®** in 51 previously treated children with severe hemophilia, aged 0 to 12 years. For 6 months, doctors studied the ABR of these children. Dosing chosen for each child aligned with their individual characteristics—either 2x/week prophylaxis (22 children) or 3x/week or every-other-day prophylaxis (29 children).[1]

SELECTED IMPORTANT SAFETY INFORMATION

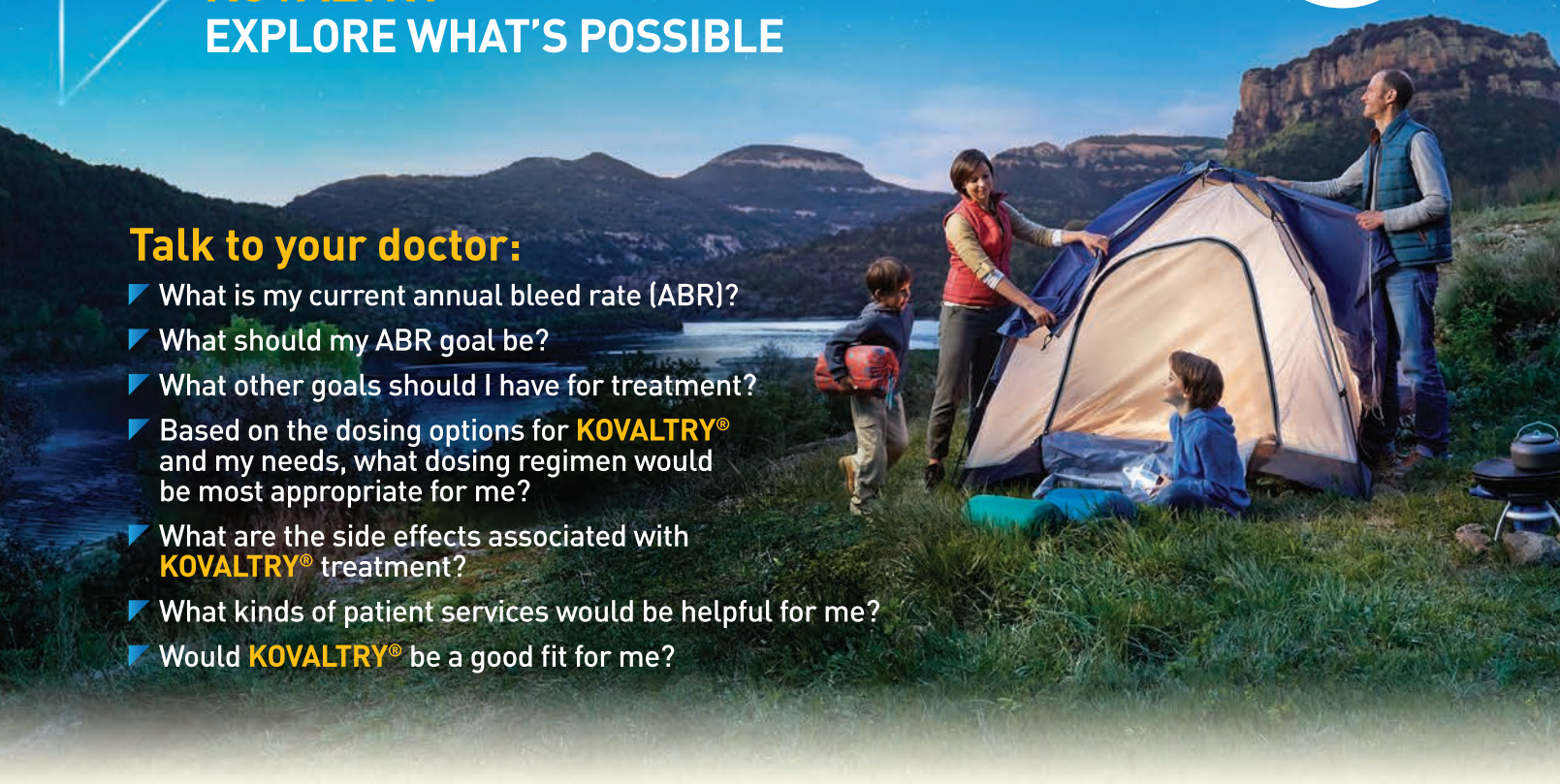
- You should not use KOVALTRY® if you are allergic to rodents (like mice and hamsters) or any ingredients in KOVALTRY®.
- Tell your healthcare provider if you have heart disease or are at risk for heart disease.
- The common side effects of KOVALTRY® are headache, fever, and itchy rash.

Please see continued Selected Important Safety Information on following page. For additional important risk and use information, please see brief summary on following pages.

Kovaltry®

Antihemophilic Factor (Recombinant)

KOVALTRY®
EXPLORE WHAT'S POSSIBLE



Talk to your doctor:

- What is my current annual bleed rate (ABR)?
- What should my ABR goal be?
- What other goals should I have for treatment?
- Based on the dosing options for KOVALTRY® and my needs, what dosing regimen would be most appropriate for me?
- What are the side effects associated with KOVALTRY® treatment?
- What kinds of patient services would be helpful for me?
- Would KOVALTRY® be a good fit for me?

Visit **www.KOVALTRY.com** to download a doctor discussion guide and other helpful information.

IMPORTANT SAFETY INFORMATION

- You should not use KOVALTRY® if you are allergic to rodents (like mice and hamsters) or any ingredients in KOVALTRY®.
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- The common side effects of KOVALTRY® are headache, fever, and itchy rash.
- Allergic reactions may occur with KOVALTRY®. Call your healthcare provider right away and stop treatment if you get tightness of the chest or throat, dizziness, decrease in blood pressure, and nausea.
- Your body can also make antibodies, called "inhibitors," against KOVALTRY®, which may stop KOVALTRY® 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.
- Tell your healthcare provider about any side effect that bothers you or that does not go away.
- Call your healthcare provider right away if bleeding is not controlled after using KOVALTRY®.

For additional important risk and use information, please see brief summary on following page.
You are encouraged to report negative side effects or quality complaints of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

References: 1. KOVALTRY® [prescribing information]. Whippany, NJ: Bayer HealthCare LLC; 2016.
2. Data on file. Bayer HealthCare Pharmaceuticals, Inc; 2016.

Kovaltry®
Antihemophilic Factor (Recombinant)

HIGHLIGHTS OF
FDA-Approved Patient Labeling

Patient Information

KOVALTRY (KOH-vahl-tree)
Antihemophilic Factor (Recombinant)

This leaflet summarizes important information about KOVALTRY with vial adapter. Please read it carefully before using this medicine. This information does not take the place of talking with your healthcare provider, and it does not include all of the important information about KOVALTRY. If you have any questions after reading this, ask your healthcare provider.

Do not attempt to self-infuse unless you have been taught how by your healthcare provider or hemophilia center.

What is KOVALTRY?

KOVALTRY 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). Hemophilia A is an inherited bleeding disorder that prevents blood from clotting normally.

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

KOVALTRY is not used to treat von Willebrand Disease.

Who should not use KOVALTRY?

You should not use KOVALTRY if you

- are allergic to rodents (like mice and hamsters).
- are allergic to any ingredients in KOVALTRY.

What should I tell my healthcare provider before I use KOVALTRY?

- Tell your healthcare provider about all of your medical conditions.
- Tell your healthcare provider and pharmacist about all of the medicines you take, including all prescription and non-prescription medicines, such as over-the-counter medicines, supplements, or herbal remedies.
- Tell your healthcare provider if you have been told you have heart disease or are at risk for heart disease.
- Tell your healthcare provider if you have been told that you have inhibitors to Factor VIII (because KOVALTRY may not work for you).

What are the possible side effects of KOVALTRY?

The common side effects of KOVALTRY are headache, fever and itchy rash.

Allergic reactions may occur with KOVALTRY. Call your healthcare provider right away and stop treatment if you get tightness of the chest or throat, dizziness, decrease in blood pressure, and nausea.

Your body can also make antibodies, called "inhibitors," against KOVALTRY, which may stop KOVALTRY 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.

These are not all the possible side effects with KOVALTRY. You can ask your healthcare provider for information that is written for healthcare professionals.

Tell your healthcare provider about any side effect that bothers you or that does not go away.

How do I store KOVALTRY?

Do not freeze KOVALTRY.

Store KOVALTRY at +2°C to +8°C (36°F to 46°F) for up to 30 months from the date of manufacture. Within this period, KOVALTRY may be stored for a period of up to 12 months at temperatures up to +25°C or 77°F.

Record the starting date of room temperature storage clearly on the unopened product carton. Once stored at room temperature, do not return the product to the refrigerator. The product then expires after storage at room temperature for 12 months, or after the expiration date on the product vial, whichever is earlier. Store vials in their original carton and protect them from extreme exposure to light.

Administer reconstituted KOVALTRY as soon as possible. If not, store at room temperature for no longer than 3 hours.

Throw away any unused KOVALTRY after the expiration date.

Do not use reconstituted KOVALTRY if it is not clear.

What else should I know about KOVALTRY and hemophilia A?

Finding veins for injections may be difficult in young children. When frequent injections are required, your healthcare provider may propose to have a device surgically placed under the skin to facilitate access to the bloodstream. These devices may result in infections.

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

This leaflet summarizes the most important information about KOVALTRY. If you would like more information, talk to your healthcare provider. You can ask your healthcare provider or pharmacist for information about KOVALTRY that was written for healthcare professionals.

Resources at Bayer available to the patient:

For Adverse Reaction Reporting, contact Bayer Medical Communications 1-888-84-BAYER (1-888-842-2937)

To receive more product information, contact KOVALTRY Customer Service 1-888-606-3780

Bayer Reimbursement HELPline 1-800-288-8374

For more information, visit www.KOVALTRY-us.com

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GOAL SETTING

When NHF and HFN became partners in WFH's Hemophilia Organization Twinning Program, the goals were clear. They included:

- Improving awareness about hemophilia and its complications across Nigeria
- Establishing a systematized advocacy effort to help influence the government to prioritize recognizing hemophilia
- Strengthening HFN's capacity to educate and reach patients

Continued from page 32

JOINING FORCES

The WFH Twinning Program was established more than 20 years ago. It advances hemophilia care in emerging countries through a formal, two-way partnership. It pairs an emerging hemophilia organization or treatment center with an established one for four years.

"Top priority for the twinning in Nigeria was to build the capacity of the patient organization, help strategize around engaging the government through advocacy and introduce a fundraising strategy," explains Rana Saifi, WFH's regional program manager for the Middle East and Africa. "NHF was deemed the best match because of its particular strengths in these areas and its close interest in sharing its knowledge and experience to help."

"It's a great honor to be part of WFH's Twinning Program," says Val D. Bias, NHF's CEO. He has hemophilia B. Bias and Neil Frick, MS, NHF's vice president for research and medical information, have made the 17-hour trip to Nigeria several times. "This is the first time that NHF has had a twinning relationship with another country," Frick says. "We felt that it was important for us to share the resources we have with organizations around the world."

THE LAY OF THE LAND

Nigeria, Africa's most populous country, is home to more than 177 million residents. The official language is English,

Continues on page 43

As part of the partnership, members of NHF and the Haemophilia Foundation of Nigeria visited the National Hospital in Abuja.

Photo Courtesy of Megan Adediran

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

Casey, a MyALPROLIX Peer,™ started on a once-every-10-day prophylaxis infusion schedule and adjusted to once every 14 days.

Learn more at www.alprolix.com/findyourfit

The recommended starting prophy regimens are either 50 IU/kg once weekly, or 100 IU/kg once every 10 days. Dosing regimen can be adjusted based on individual response.

Children under 12 years of age may have higher Factor IX body weight-adjusted clearance, shorter half-life, and lower recovery. Higher dose per kilogram body weight or more frequent dosing may be needed in these children.

Extended protection* from bleeds

ALPROLIX is the first factor IX offering prophylaxis infusion schedules starting every 7 or 10 days with the potential to extend based on your response.

*ALPROLIX has been proven to help patients prevent bleeding episodes using a prophylaxis regimen.

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:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding
- Routine prophylaxis to 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. This information is not intended to replace discussions with your healthcare provider.

Biogen

FIX-US-0573 V2 03/2016

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.

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Continued from page 40

but residents may speak up to three additional languages (or one or more of more than 500 indigenous languages). Further, they can be members of more than 250 ethnic groups.

Because populations are diverse, traditions can be as well. For instance, in addition to circumcision, some communities have their infants' uvulas (the flap of tissue at the back of the throat) removed as a ritual custom. "Babies with undiagnosed hemophilia have died from these procedures without anyone knowing why," Adediran says.

Obstacles include travel distances and expenses. People generally need to pay out of pocket for any treatments they receive, as government entities (which provide health care in Nigeria) do not currently recognize hemophilia in their policies.

"Nigeria is a difficult country for people with hemophilia at best, and the need is tremendous," Bias says. He was moved by the economic disparity he saw, recalling the many Nigerian vendors on the sides of roads who sold everything from fruit to furniture to make ends meet.

When the team began to meet with families of more than 100 patients, needs became even clearer. "All the families we met had lost at least one child to a bleeding disorder due to the lack of treatment and diagnosis," Bias says.

BUILDING A NETWORK

The improvements in HFN's ability to provide patient education programs and expand awareness are evident. "It is now the go-to source for all Nigerian patients," Saifi says. "Its outreach work has ensured that patients in remote areas have access to treatment." Further, HFN now works closely with about 10 hemophilia treatment centers (HTCs) across Nigeria, she adds.

NHF and HFN collaborated on drafting letters to local, state and federal governments to educate leaders on hemophilia. They also helped strengthen local chapters across Nigeria by providing training on fundraising and board development.

In addition, NHF provided training and needed infrastructure to Adediran's foundation and to medical staff. NHF also trained a number of clinicians in diagnosis and treatment.

Further, NHF helped craft health messages, including one that explained the importance of the RICE (rest, ice, compression and elevation) method of treating bleeds, particularly in the absence of factor products. "Every patient we saw there had joint bleeds or damage," Frick explains. "Although the national hospital had outdated equipment, it did have dedicated doctors."

> "THIS IS THE FIRST TIME THAT NHF HAS HAD A TWINNING RELATIONSHIP WITH ANOTHER COUNTRY. WE FELT THAT IT WAS IMPORTANT FOR US TO SHARE THE RESOURCES WE HAVE WITH ORGANIZATIONS AROUND THE WORLD."

The Twinning Program does not allow for the distribution of treatment products. But some hospitals in Nigeria use supplies donated through the WFH Humanitarian Aid Program, Adediran says. "Despite much progress in the dialogue, there is still some way to go to fully influence the government of Nigeria to recognize hemophilia in its policies and provide treatment products," Saifi says.

Still, the program's accomplishments are clear. "The thing I'm most proud of is that more people know about hemophilia than when we first got there," Frick says. "And progress continues. For instance, the Children's Hospital of Philadelphia HTC is now a medical twinning partner for the University of Nigeria Teaching Hospital."

NEVER-ENDING RELATIONSHIP

Bias and Frick confirm NHF will continue to be a resource, even when the formal partnership ends. "I'm talking with the NHF Board about providing ongoing support to Nigeria," Bias says. In addition, NHF is encouraging its chapters to partner with other emerging countries through the Twinning Program. Bias notes that NHF may underwrite some of HFN's costs.

Adediran is looking ahead to continued work with NHF and continued advocacy in her home country. "Before the foundation, there was no hope," she says. With NHF's help, HFN has become a more developed organization. "Through NHF, I've become a better advocate to the community," Adediran adds. "And we've been able to develop a lot of education."

After numerous Skype calls and telephone chats, in addition to in-person visits, the NHF and HFN relationship remains strong. "I admire Meagan Adediran and her husband," Bias says. He's impressed that Adediran finances the work of the foundation partly out of her own pocket. "This relationship will never end," adds Frick. "We'll always be there to support HFN and its founder." ●

- Read more about the World Federation of Hemophilia's Twinning Program: www.wfh.org/en/twins
- Visit the Haemophilia Foundation of Nigeria's website, which includes details on how you can be involved: haemocare.org.ng
- Review advocacy resources and tools from the National Hemophilia Foundation: hemophilia.org/Advocacy-Healthcare-Coverage/Advocacy-Tools-Resources

Independence Days

Time to take ownership of your healthcare

BY MIKE CARLSON

Little about the growing-up experience is easy for children or parents. If you're a young adult with a bleeding disorder, the transition from relying on parents to manage your care to sudden—and required—self-reliance is just another step in a dizzying sequence of life-changing events.

"Change is hard," says Stacy Croteau, MD, MMS, instructor of pediatrics at Harvard Medical School. She is also associate director of the Boston Hemophilia Center, where she sees patients who range in age from infancy to their mid-20s. "When young adults have the option of continuing to do what they have done since childhood or transferring care to a new clinic with new providers, it isn't surprising they usually choose to stick with what is working for them and confront change only when they have to."

Still, change is inevitable. "When my son was 15, I realized he had never ordered his own factor. I teach on this topic, yet my own kid was not doing it," says Dawn Rotellini, senior vice president of chapter development and education at the National Hemophilia Foundation (NHF). She is also a member of NHF's Transition Committee. Her son, Gino, now 18, has moderate hemophilia A.

Managing this transition to self-care is best done slowly, in stages. Even if out-of-state college is months away, there are several steps to help you feel comfortable caring for your condition on your own.

Only on hemaware.org: Five things to bring to your first solo adult health appointment.

XiXinXing/Thinkstock

Step by step

The transition to adult treatment is a big step, but it's not the first. Ideally, your care journey is marked by small successes. Rungs in the ladder may include helping set up your infusion equipment when you were a toddler, self-infusing in middle school and donning your MedicAlert® bracelet in high school.

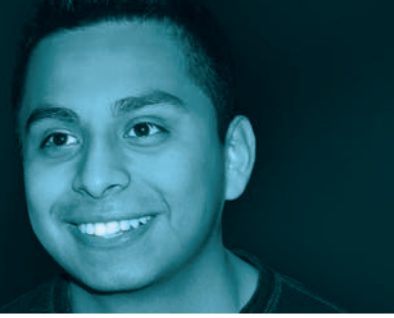
Several programs and resources help families chart the course to independence. NHF's Steps for Living website provides advice and resources for all life stages, from childhood to adolescence and adulthood. Another resource is the HEMO-milestones Tool, a standardized evaluation of a patient's self-care skills. It assesses the patient from birth, when parents manage care, through adolescence, when the teen assumes more responsibility for care and treatment. By recognizing significant accomplishments, such as self-infusion skills, medical knowledge and the ability to communicate with healthcare professionals, the tools can help instill confidence and competency in young adults.

"The HEMO-milestones Tool helps us understand where on that path to medical independence patients and their parents are," says Croteau, who helped create it. "We can support their skill level and help them progress to the next step."

Continues on page 47

IXINITY®
coagulation factor IX (recombinant)

NATHAN'S IXperience™



Nathan and his doctor discussed the **98% RECOVERY[1]*** of IXINITY

HE'S INFUSING 4,000 IU* with IXINITY—less than in the past

He thinks the IXINITY reconstitution device is **EASY TO USE**

"When I heard the recovery rate was 98%, I thought, 'Wow, that's pretty close to the recovery of a plasma-derived product'."

Watch Nathan's videos at PatientIXperiences.com

Nathan's experience with IXINITY may not be typical. Speak with your doctor to see if IXINITY may be a good option for you.

*Nathan uses 4000 IU per infusion. IXINITY recovery is an average based on lab tests of patients in the clinical study.[1] Your actual recovery and dose may be different. Speak with your healthcare professional about the right dose for you.

INDICATIONS AND IMPORTANT SAFETY INFORMATION

What is IXINITY®?

IXINITY [coagulation factor IX (recombinant)] is a medicine used to replace clotting factor (factor IX) that is missing in adults and children at least 12 years of age with hemophilia B. Hemophilia B is also called congenital factor IX deficiency or Christmas disease. Hemophilia B is an inherited bleeding disorder that prevents clotting. Your healthcare provider may give you IXINITY to control and prevent bleeding episodes or when you have surgery.

IXINITY is not indicated for induction of immune tolerance in patients with Hemophilia B.

IMPORTANT SAFETY INFORMATION FOR IXINITY®

- You should not use IXINITY if you are allergic to hamsters or any ingredients in IXINITY.
- You should tell your healthcare provider if you have or have had 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 experience an allergic reaction to IXINITY. Contact your health-care provider or get emergency treatment right away if you develop 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 IXINITY. An inhibitor is part of the body's defense system. If you develop inhibitors, it may prevent IXINITY from working properly. Consult with your healthcare provider to make sure you are carefully monitored with blood tests for development of inhibitors to IXINITY.
- If you have risk factors for developing blood clots, the use of IXINITY may increase the risk of abnormal blood clots.
- Call your healthcare provider right away about any side effects that bother you or do not go away, or if your bleeding does not stop after taking IXINITY.
- The most common side effect that was reported with IXINITY during clinical trials was headache.
- These are not all the side effects possible with IXINITY. You can ask your healthcare provider for information that is written for healthcare professionals.

You are encouraged to report side effects of prescription drugs to the Food and Drug Administration. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see accompanying brief summary of Prescribing Information on next page.

Reference: 1. IXINITY [coagulation factor IX (recombinant)] prescribing information. Winnipeg, MB, Canada; Emergent BioSolutions Inc.; April 2015.

Manufactured by Cangene Corporation, a subsidiary of Emergent BioSolutions Inc. and distributed by Cangene bioPharma, Inc., a subsidiary of Emergent BioSolutions Inc.

emergent biosolutions®

IXINITY®
coagulation factor IX
(recombinant)

Factoring in your world™

IXINITY® [coagulation factor IX (recombinant)]

Brief Summary for the Patient

See package insert for full Prescribing Information. This product's label may have been updated. For further product information and current package insert, please visit www.IXINITY.com.

Please read this Patient Information carefully before using IXINITY. This brief summary does not take the place of talking with your healthcare provider, and it does not include all of the important information about IXINITY.

What is IXINITY?

IXINITY is a medicine used to replace clotting factor (factor IX) that is missing in people with hemophilia B. Hemophilia B is also called congenital factor IX deficiency or Christmas disease. Hemophilia B is an inherited bleeding disorder that prevents clotting. Your healthcare provider may give you IXINITY when you have surgery.

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

Who should not use IXINITY?

You should not use IXINITY if you:

- Are allergic to hamsters
- Are allergic to any ingredients in IXINITY

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

What should I tell my healthcare provider before using IXINITY?

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 breastfeeding. It is not known if IXINITY passes into your milk and if it can harm your baby
- Are pregnant or planning to become pregnant. It is not known if IXINITY may harm your baby
- Have been told that you have inhibitors to factor IX (because IXINITY may not work for you)

How should I infuse IXINITY?

IXINITY is given directly into the bloodstream. IXINITY should be administered as ordered by your healthcare provider. You should be trained on how to do infusions by your healthcare provider or hemophilia treatment center. Many people with hemophilia B learn to infuse their IXINITY by themselves or with the help of a family member.

See the step-by-step instructions for infusing in the complete patient labeling.

Your healthcare provider will tell you how much IXINITY to use based on your weight, the severity of your hemophilia B, and where you are bleeding. You may have to have blood tests done after getting IXINITY to be sure that your blood level of factor IX is high enough to stop the bleeding. Call your healthcare provider right away if your bleeding does not stop after taking IXINITY.

What are the possible side effects of IXINITY?

Allergic reactions may occur with IXINITY. Call your healthcare provider or get emergency treatment right away if you have any of the following symptoms:

- Rash
- Hives
- Itching
- Tightness of the throat
- Chest pain or tightness
- Difficulty breathing
- Lightheadedness
- Dizziness
- Nausea
- Fainting

Tell your healthcare provider about any side effect that bothers you or does not go away.

The most common side effect of IXINITY in clinical trials was headache.

These are not all of the possible side effects of IXINITY. You can ask your healthcare provider for information that is written for healthcare professionals.

Call your healthcare provider for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

How should I store IXINITY?

Store IXINITY at 2 to 25°C (36 to 77°F). Do not freeze.

Do not use IXINITY after the expiration date printed on the label. Throw away any unused IXINITY and diluents after it reaches this date.

Reconstituted product (after mixing dry product with Sterile Water for Injection) must be used within 3 hours and cannot be stored or refrigerated. Discard any IXINITY left in the vial at the end of your infusion.

Do not use IXINITY if the reconstituted solution is not clear and colorless.

What else should I know about IXINITY?

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

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

Always check the actual dosage strength printed on the label to make sure you are using the strength prescribed by your healthcare provider.

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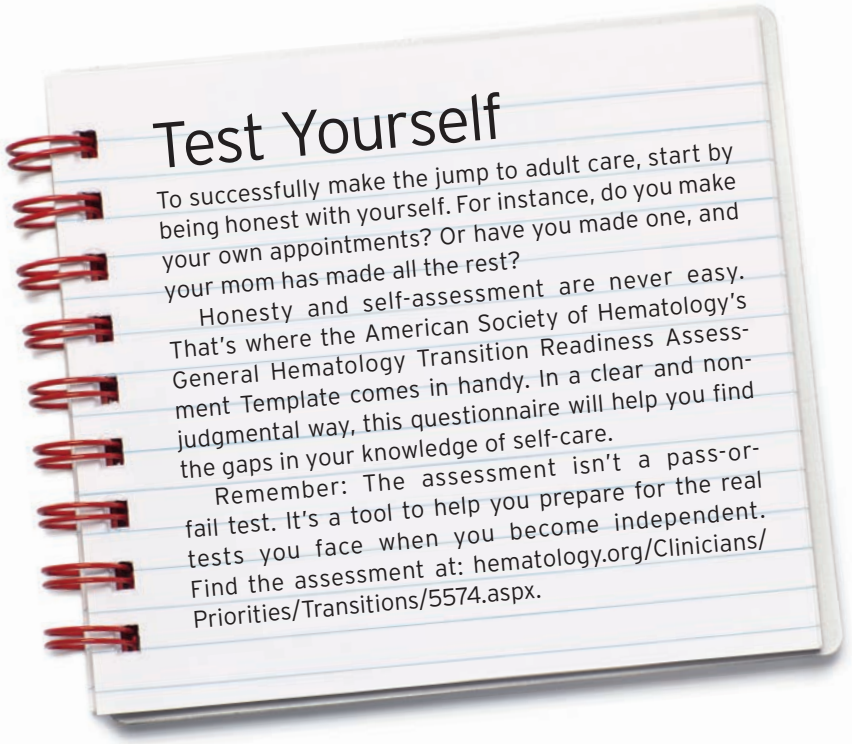

Continued from page 44

Community programs and activities are other valuable resources, says Rotellini. Conferences and fundraising events provide a safe place to meet peers living with the same or similar bleeding disorders, to ask questions and even to pick up a few tips. "Kids and families who attend chapter activities get a lot of education," Rotellini says. "They're exposed to other kids with bleeding disorders and can watch how they behave."

For many adolescents and teens, summer camp is the first time they're put in charge of their own care. Sleepaway camps encourage and celebrate self-infusing, with tangible rewards like certificates and prizes. In addition, older counselors serve as role models and mentors to the kids in their cabins.

Check yourself

To better understand where you fall on your quest for independence, take the American Society of Hematology's (ASH's) General Hematology Transition Readiness Assessment Template. Patients rate themselves on 22 statements across five categories. Statements include: "I can fill out a medical history form," "I understand my insurance plan" and "I know what to do in case of a medical emergency." (See sidebar, "Test Yourself.")

Consider the tool a snapshot of where you are today. Let it show you where you need to get answers and focus your efforts. Discuss the assessment with your parents, your hemophilia treatment center (HTC) care team and your primary care physician.

Talk about it

Croteau has found that patients with severe bleeding disorders are extremely knowledgeable about their own conditions and treatment, more so than her patients with moderate forms. However, most of the young people she works with struggle with the communication part of the puzzle. You can start practicing communication skills in high school. That's a good time to begin making your own doctor's appointments and ordering your own supplies.

Sit down together with your family to review insurance paperwork and billing. Start with the basics, such as defining terms like deductible, copayment and formulary. Ask questions.

If you're heading to a college away from home, discuss insurance coverage, and how to order factor and have it delivered. Locate the HTC and hospital closest to your college campus. Add them as contacts in your phone.

Find your motivation

You may benefit from having an incentive. For Gino, who had been putting off practicing his self-infusion skills, it was a high school band trip. "I told him, 'I'm not going to be there to infuse you. If you can't take care of your own bleeding disorder, you can't go on this trip,'" his mom says. That's all the motivation Gino needed. Now he's in college and self-infuses.

Travel was also the impetus for Nikole Scappe, of Coraopolis, Pennsylvania, to take her self-care skills to the next level. A member of NHF's Board of Directors and the 2015 recipient of NHF's Ryan White Award, the 25-year-old college student has been handling her own treatment for von Willebrand disease since she was 18. Still, while planning a trip to Italy last year, she discovered an even greater level of comfort with her treatment plan. Scappe tapped into the multitude of resources available. A member of an online women's group for bleeding disorders had recently helped her daughter plan a similar trip and offered plenty of advice. Scappe also reached out to her HTC. "The social worker shared a lot of research with me," she says. "She helped me put all the information in my travel letter."

Whatever your motivation, use the resources available to you at your HTC and in the community to prepare to reach your next goal. ●

- For additional healthcare transition resources: gottransition.org/resources
- NHF's Steps for Living website: stepsforliving.hemophilia.org
- The Dana-Farber/Boston Children's Cancer and Blood Disorders Center HEMO-milestones program: ncbi.nlm.nih.gov/pubmed/26496140

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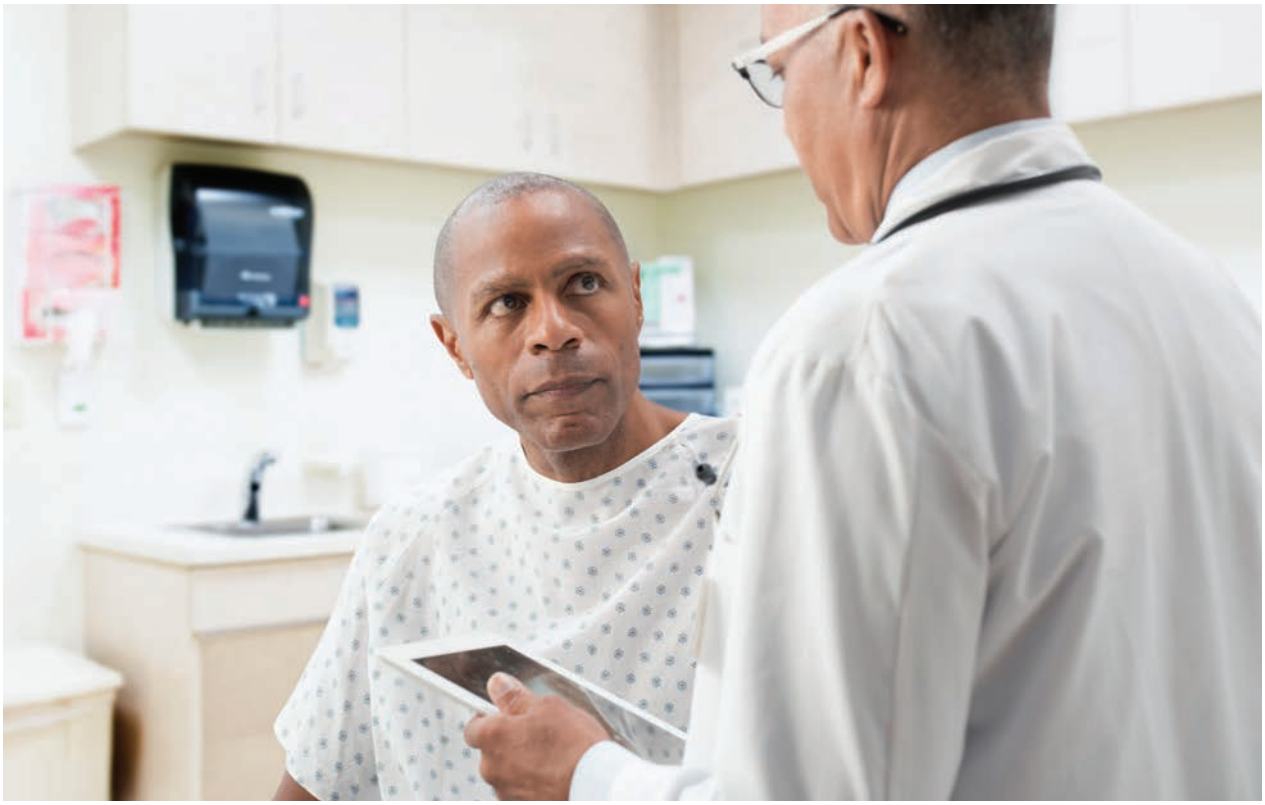

Listen to Your Liver Doc

Follow-up care after curing hep C

BY SARAH M. ALDRIDGE, MS

You've waited more than 20 years to hear the words: "You are cured." Now that the hepatitis C virus (HCV) infection is behind you, your future liver health is up to you. If you ignore doctors' orders and party like a college kid, you will add insult to the injury that's been done for decades.

"Our worst fear is that patients with advanced liver fibrosis (scarring) will drop out of the healthcare system, thinking that they're cured," says Bruce Luxon, MD, PhD, Anton and Margaret Fuisz Chair in Medicine, chairman and physician in chief, Department of Medicine, Georgetown University. "Indeed, they are cured of their hepatitis C, but they still have liver disease," says Luxon, a member of the National Hemophilia Foundation's Medical and Scientific Advisory Council (MASAC). Follow your liver doctor's recommendations for follow-up care and lifestyle changes.

Liver recovery

The development of direct-acting antivirals (DAA), combination oral drugs that disrupt proteins HCV needs to reproduce, has dramatically improved the outlook for all patients. That includes people with hemophilia and HCV, who previously hadn't been cured at the rate of the general public. "Now our goal is to cure everybody," Luxon says. By "cure," he means achieving sustained virologic response (SVR), where there is no detectable viral load (HCV RNA) in the blood 12 weeks after treatment ends.

Clearing the body of HCV has significant health benefits. "That is extremely exciting because we may be impacting diabetes, atherosclerosis and cardiovascular disease, stroke risk and renal disease," says Kenneth Sherman, MD, PhD, Gould Professor of Medicine and director of the Division of Digestive Diseases at the University of Cincinnati College of Medicine.

But being told you're cured is only the first step in a long recovery process. How your liver and other organs rebound after SVR depends on the extent of fibrosis and complications beforehand. "Fibrosis (liver scarring from chronic HCV infection and inflammation) takes, on the average, 10 to 20 years to develop," Luxon says. "It takes another 10 to 20 years to go away."

Continues on page 51

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Amicar®
(aminocaproic acid)
Oral Solution and Tablets

Enhancing hemostasis when fibrinolysis contributes to bleeding.

move freely

See Important Safety Information below and full prescribing information on reverse side.

INDICATIONS AND USAGE

AMICAR is useful in enhancing hemostasis when fibrinolysis contributes to bleeding. In life-threatening situations, transfusion of appropriate blood products and other emergency measures may be required. Fibrinolytic bleeding may frequently be associated with surgical complications following heart surgery (with or without cardiac bypass procedures) and portacaval shunt; hematological disorders such as amegakaryocytic thrombocytopenia (accompanying aplastic anemia); acute and life-threatening abruptio placentae; hepatic cirrhosis; and neoplastic disease such as carcinoma of the prostate, lung, stomach, and cervix. Urinary fibrinolysis, usually a normal physiological phenomenon, may contribute to excessive urinary tract fibrinolytic bleeding associated with surgical hematuria (following prostatectomy and nephrectomy) or nonsurgical hematuria (accompanying polycystic or neoplastic diseases of the genitourinary system).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

AMICAR should not be used when there is evidence of an active intravascular clotting process. When there is uncertainty as to whether the cause of bleeding is primary fibrinolysis or disseminated intravascular coagulation (DIC), this distinction must be made before administering AMICAR. AMICAR must not be used in the presence of DIC without concomitant heparin.

WARNINGS

- In patients with upper urinary tract bleeding, AMICAR administration has been known to cause intrarenal obstruction in the form of glomerular capillary thrombosis or clots in the renal pelvis and ureters. For this reason, AMICAR should not be used in hematuria of upper urinary tract origin, unless the possible benefits outweigh the risk.
- Subendocardial hemorrhages have been observed in dogs given intravenous infusions of 0.2 times the maximum human therapeutic dose of AMICAR and in monkeys given 8 times the maximum human therapeutic dose of AMICAR.
- Fatty degeneration of the myocardium has been reported in dogs given intravenous doses of AMICAR at 0.8 to 3.3 times the maximum human therapeutic dose and in monkeys given intravenous doses of AMICAR at 6 times the maximum human therapeutic dose.
- Rarely, skeletal muscle weakness with necrosis of muscle fibers has been reported following prolonged administration. Clinical presentation may range from mild myalgias with weakness and fatigue to a severe proximal myopathy with rhabdomyolysis, myoglobinuria, and acute renal failure. Muscle enzymes, especially creatine phosphokinase (CPK) are elevated. CPK levels should be monitored in patients on long-term therapy. AMICAR administration should be stopped if a rise in CPK is noted.
- The possibility of cardiac muscle damage should also be considered when skeletal myopathy occurs. One case of cardiac and hepatic lesions observed in man has been reported. The patient received 2 g of aminocaproic acid every 6 hours for a total dose of 26 g. Death was due to continued cerebrovascular hemorrhage. Necrotic changes in the heart and liver were noted at autopsy.

ADVERSE REACTIONS

AMICAR is generally well tolerated. The following adverse experiences have been reported:

- **General:** Edema, headache, malaise.
- **Hypersensitivity Reactions:** Allergic and anaphylactoid reactions, anaphylaxis.
- **Cardiovascular:** Bradycardia, hypotension, peripheral ischemia, thrombosis.
- **Gastrointestinal:** Abdominal pain, diarrhea, nausea, vomiting.
- **Hematologic:** Agranulocytosis, coagulation disorder, leukopenia, thrombocytopenia.
- **Musculoskeletal:** CPK increased, muscle weakness, myalgia, myopathy (see WARNINGS), myositis, rhabdomyolysis.
- **Neurologic:** Confusion, convulsions, delirium, dizziness, hallucinations, intracranial hypertension, stroke, syncope.
- **Respiratory:** Dyspnea, nasal congestion, pulmonary embolism.
- **Skin:** Pruritis, rash.
- **Special Senses:** Tinnitus, vision decreased, watery eyes.
- **Urogenital:** BUN increased, renal failure. There have been some reports of dry ejaculation during the period of AMICAR treatment. These have been reported to date only in hemophilia patients who received the drug after undergoing dental surgical procedures. However, this symptom resolved in all patients within 24 to 48 hours of completion of therapy.

Patient support programs are available. To learn more, visit: amicar.org/patient-assistance-program/

AKORN

www.amicar.org

Amicar®
(aminocaproic acid)
Oral Solution and Tablets

AMICAR® (aminocaproic acid) Oral Solution and Tablets
Rx only

DESCRIPTION

AMICAR (aminocaproic acid) is 6-aminohexanoic acid, which acts as an inhibitor of fibrinolysis.
Its chemical structure is:

$$H_2C(CH_2)_3CH_2COOH$$
$$|$$
$$NH_2$$

$C_6H_{13}NO_2$ M.W. 131.17

AMICAR is soluble in water, acid, and alkaline solutions; it is sparingly soluble in methanol and practically insoluble in chloroform.

AMICAR (aminocaproic acid) Oral Solution for oral administration, contains 0.25 g/mL of aminocaproic acid with methylparaben 0.20%, propylparaben 0.05%, edetate disodium 0.30% as preservatives and the following inactive ingredients: sodium saccharin, sorbitol solution, citric acid anhydrous, natural and artificial raspberry flavor and an artificial bitterness modifier.

Each AMICAR (aminocaproic acid) Tablet, for oral administration contains 500 mg or 1000 mg of aminocaproic acid and the following inactive ingredients: povidone, crospovidone, stearic acid, and magnesium stearate.

CLINICAL PHARMACOLOGY

The fibrinolysis-inhibitory effects of AMICAR appear to be exerted principally via inhibition of plasminogen activators and to a lesser degree through antiplasmin activity.

In adults, oral absorption appears to be a zero-order process with an absorption rate of 5.2 g/hr. The mean lag time in absorption is 10 minutes. After a single oral dose of 5 g, absorption was complete (F=1). Mean ± SD peak plasma concentrations (164 ± 28 mcg/mL) were reached within 1.2 ± 0.45 hours.

After oral administration, the apparent volume of distribution was estimated to be 23.1 ± 6.6 L (mean ± SD). Correspondingly, the volume of distribution after intravenous administration has been reported to be 30.0 ± 8.2 L. After prolonged administration, AMICAR has been found to distribute throughout extravascular and intravascular compartments of the body, penetrating human red blood cells as well as other tissue cells.

Renal excretion is the primary route of elimination. Sixty-five percent of the dose is recovered in the urine as unchanged drug and 11% of the dose appears as the metabolite adipic acid. Renal clearance (116 mL/min) approximates endogenous creatinine clearance. The total body clearance is 169 mL/min. The terminal elimination half-life for AMICAR is approximately 2 hours.

INDICATIONS AND USAGE

AMICAR is useful in enhancing hemostasis when fibrinolysis contributes to bleeding. In life-threatening situations, transfusion of appropriate blood products and other emergency measures may be required.

Fibrinolytic bleeding may frequently be associated with surgical complications following heart surgery (with or without cardiac bypass procedures) and portacaval shunt; hematological disorders such as amegakaryocytic thrombocytopenia (accompanying aplastic anemia); acute and life-threatening abruptio placentae; hepatic cirrhosis; and neoplastic disease such as carcinoma of the prostate, lung, stomach, and cervix.

Urinary fibrinolysis, usually a normal physiological phenomenon, may contribute to excessive urinary tract fibrinolytic bleeding associated with surgical hematuria (following prostatectomy and nephrectomy) or nonsurgical hematuria (accompanying polycystic or neoplastic diseases of the genitourinary system). (See **WARNINGS**.)

CONTRAINDICATIONS

AMICAR should not be used when there is evidence of an active intravascular clotting process. When there is uncertainty as to whether the cause of bleeding is primary fibrinolysis or disseminated intravascular coagulation (DIC), this distinction must be made before administering AMICAR.

The following tests can be applied to differentiate the two conditions: Platelet count is usually decreased in DIC but normal in primary fibrinolysis. Protamine paracoagulation test is positive in DIC; a precipitate forms when protamine sulfate is dropped into citrated plasma. The test is negative in the presence of primary fibrinolysis. The euglobulin clot lysis test is abnormal in primary fibrinolysis but normal in DIC.

AMICAR must not be used in the presence of DIC without concomitant heparin.

WARNINGS

In patients with upper urinary tract bleeding, AMICAR administration has been known to cause intrarenal obstruction in the form of glomerular capillary thrombosis or clots in the renal pelvis and ureters. For this reason, AMICAR should not be used in hematuria of upper urinary tract origin, unless the possible benefits outweigh the risk.

Subendocardial hemorrhages have been observed in dogs given intravenous infusions of 0.2 times the maximum human therapeutic dose of AMICAR and in monkeys given 8 times the maximum human therapeutic dose of AMICAR.

Fatty degeneration of the myocardium has been reported in dogs given intravenous doses of AMICAR at 0.8 to 3.3 times the maximum human therapeutic dose and in monkeys given intravenous doses of AMICAR at 6 times the maximum human therapeutic dose.

Rarely, skeletal muscle weakness with necrosis of muscle fibers has been reported following prolonged administration. Clinical presentation may range from mild myalgias with weakness and fatigue to a severe proximal myopathy with rhabdomyolysis, myoglobinuria, and acute renal failure. Muscle enzymes, especially creatine phosphokinase (CPK) are elevated. CPK levels should be monitored in patients on long-term therapy. AMICAR administration should be stopped if a rise in CPK is noted. Resolution follows discontinuation of AMICAR; however, the syndrome may recur if AMICAR is restarted.

The possibility of cardiac muscle damage should also be considered when skeletal myopathy occurs. One case of cardiac and hepatic lesions observed in man has been reported. The patient received 2 g of aminocaproic acid every 6 hours for a total dose of 26 g. Death was due to continued cerebrovascular hemorrhage. Necrotic changes in the heart and liver were noted at autopsy.

PRECAUTIONS

General

AMICAR inhibits both the action of plasminogen activators and to a lesser degree, plasmin activity. The drug should NOT be administered without a definite diagnosis and/or laboratory finding indicative of hyperfibrinolysis (hyperplasminemia). Inhibition of fibrinolysis by aminocaproic acid may theoretically result in clotting or thrombosis. However, there is no definite evidence that administration of aminocaproic acid has been responsible for the few reported cases of intravascular clotting which followed this treatment. Rather, it appears that such intravascular clotting was most likely due to the patient's preexisting clinical condition, e.g., the presence of DIC. It has been postulated that extravascular clots formed *in vivo* may not undergo spontaneous lysis as do normal clots.

Reports have appeared in the literature of an increased incidence of certain neurological deficits such as hydrocephalus, cerebral ischemia, or cerebral vasospasm associated with the use of antifibrinolytic agents in the treatment of subarachnoid hemorrhage (SAH). All of these events have also been described as part of the natural course of SAH, or as a consequence of diagnostic procedures such as angiography. Drug relatedness remains unclear.

Aminocaproic acid should not be administered with Factor IX Complex concentrates or Anti-Inhibitor Coagulant concentrates, as the risk of thrombosis may be increased.

Laboratory Tests

The use of AMICAR should be accompanied by tests designed to determine the amount of fibrinolysis present. There are presently available: (a) general tests such as those for the determination of the lysis of a clot of blood or plasma; and (b) more specific tests for the study of various phases of the fibrinolytic mechanisms. These latter tests include both semiquantitative and quantitative techniques for the determination of profibrinolysin, fibrinolysin, and antifibrinolysin.

Drug Laboratory Test Interactions

Prolongation of the template bleeding time has been reported during continuous intravenous infusion of AMICAR at dosages exceeding 24 g/day. Platelet function studies in these patients have not demonstrated any significant platelet dysfunction. However, *in vitro* studies have shown that at high concentrations (7.4 mMol/L or 0.97 mg/mL and greater) aminocaproic acid inhibits ADP and collagen-induced platelet aggregation, the release of ATP and serotonin, and the binding of fibrinogen to the platelets in a concentration-response manner. Following a 10 g bolus of AMICAR, transient peak plasma concentrations of 4.6 mMol/L or 0.60 mg/mL have been obtained. The concentration of AMICAR necessary to maintain inhibition of fibrinolysis is 0.99 mMol/L or 0.13 mg/mL. Administration of a 5 g bolus followed by 1 to 1.25 g/hr should achieve and sustain plasma levels of 0.13 mg/mL.Thus, concentrations which have been obtained *in vivo* clinically in patients with normal renal function are considerably lower than the *in vitro* concentrations found to induce abnormalities in platelet function tests. However, higher plasma concentrations of AMICAR may occur in patients with severe renal failure.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate the carcinogenic potential of AMICAR and studies to evaluate its mutagenic potential have not been conducted. Dietary administration of an equivalent of the maximum human therapeutic dose of AMICAR to rats of both sexes impaired fertility as evidenced by decreased implantations, litter sizes and number of pups born.

Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with AMICAR. It is also not known whether AMICAR can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. AMICAR should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when AMICAR is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

AMICAR is generally well tolerated. The following adverse experiences have been reported:

General: Edema, headache, malaise.

Hypersensitivity Reactions: Allergic and anaphylactoid reactions, anaphylaxis.

Cardiovascular: Bradycardia, hypotension, peripheral ischemia, thrombosis.

Gastrointestinal: Abdominal pain, diarrhea, nausea, vomiting.

Hematologic: Agranulocytosis, coagulation disorder, leukopenia, thrombocytopenia.

Musculoskeletal: CPK increased, muscle weakness, myalgia, myopathy (see **WARNINGS**), myositis, rhabdomyolysis.

Neurologic: Confusion, convulsions, delirium, dizziness, hallucinations, intracranial hypertension, stroke, syncope.

Respiratory: Dyspnea, nasal congestion, pulmonary embolism.

Skin: Pruritis, rash.

Special Senses: Tinnitus, vision decreased, watery eyes.

Urogenital: BUN increased renal failure. There have been some reports of dry ejaculation during the period of AMICAR treatment. These have been reported to date only in hemophilia patients who received the drug after undergoing dental surgical procedures. However, this symptom resolved in all patients within 24 to 48 hours of completion of therapy.

OVERDOSAGE

A few cases of acute overdosage with AMICAR administered intravenously have been reported. The effects have ranged from no reaction to transient hypotension to severe acute renal failure leading to death. One patient with a history of brain tumor and seizures experienced seizures after receiving an 8 gram bolus injection of AMICAR. The single dose of AMICAR causing symptoms of overdosage or considered to be life-threatening is unknown. Patients have tolerated doses as high as 100 grams while acute renal failure has been reported following a dose of 12 grams.

The intravenous and oral LD50 of AMICAR were 3.0 and 12.0 g/kg, respectively, in the mouse and 3.2 and 16.4 g/kg, respectively, in the rat. An intravenous infusion dose of 2.3 g/kg was lethal in the dog. On intravenous administration, tonic-clonic convulsions were observed in dogs and mice.

No treatment for overdosage is known, although evidence exists that AMICAR is removed by hemodialysis and may be removed by peritoneal dialysis. Pharmacokinetic studies have shown that total body clearance of AMICAR is markedly decreased in patients with severe renal failure.

DOSAGE AND ADMINISTRATION

An identical dosage regimen may be followed by administering AMICAR Tablets or AMICAR Oral Solution as follows:

For the treatment of acute bleeding syndromes due to elevated fibrinolytic activity, it is suggested that 5 AMICAR 1000 mg Tablets or 10 AMICAR 500 mg Tablets (5 g) or 20 milliliters of AMICAR Oral Solution (5 g) be administered during the first hour of treatment, followed by a continuing rate of 1 AMICAR 1000 mg Tablet or 2 AMICAR 500 mg Tablets (1 g) or 5 milliliters of AMICAR Oral Solution (1.25 g) per hour. This method of treatment would ordinarily be continued for about 8 hours or until the bleeding situation has been controlled.

HOW SUPPLIED:

AMICAR®
(aminocaproic acid)
AMICAR Oral Solution, 0.25 g/mL
Each mL of raspberry-flavored oral solution contains 0.25 g/mL of aminocaproic acid.
8 Fl. Oz. (236.5 mL) Bottle – NDC 49411-052-08
Store at 20°-25°C (68°-77°F)[see USP Controlled Room Temperature]; Dispense in Tight Containers; Do Not Freeze.

AMICAR 500 mg Tablets
Each round, white tablet, engraved with XP on one side and scored on the other with A to the left of the score and 10 on the right, contains 500 mg of aminocaproic acid.
Bottle of 30 – NDC 49411-050-30
Store at 20°-25°C (68°-77°F)[see USP Controlled Room Temperature]; Dispense in Tight Containers; Do Not Freeze.

AMICAR 1000 mg Tablets
Each oblong, white tablet, engraved with XP on one side and scored on the other with A to the left of the score and 20 on the right, contains 1000 mg of aminocaproic acid.
Bottle of 30 – NDC 49411-051-30
Store at 20°-25°C (68°-77°F)[see USP Controlled Room Temperature]; Dispense in Tight Containers; Do Not Freeze.

REFERENCE

[1]Stefanini M, Dameshek W: *The Hemorrhagic Disorders*, Ed. 2, New York, Grune and Stratton; 1962: 510-514.

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Continued from page 48

Lifestyle changes

Over-the-counter drugs and beverages containing alcohol can damage your liver. Stay below the 2,000 mg-per-day limit for acetaminophen, a pain reliever commonly recommended for people with bleeding disorders, say liver specialists.

Think twice about knocking back a cold one. "If you have advanced fibrosis, avoid alcohol for sure," Luxon says. Tattoos and piercings may be popular, but they should be considered cautiously. "Any type of skin breakage with potentially contaminated materials poses a risk for reinfection with hep C," warns Sherman.

Follow-up medical care

A hepatologist, or liver specialist, is the preferred provider when it comes to liver diseases. He or she will advise you of what tests and screenings you'll need, and how often. Remember: If you have advanced fibrosis or cirrhosis, you will be followed much more closely.

The most accurate measure of liver fibrosis is the METAVIR score. It ranges from F0, no scarring, to F4, cirrhosis. It can be obtained without the invasiveness of a biopsy, using FibroScan®. This device bounces sound waves off the liver, determining how stiff, or fibrotic, it is.

Hepatocellular carcinoma (HCC), a type of liver cancer, is another condition to monitor. "The risk of liver cancer continues in a person with cirrhosis, even after an SVR," Luxon stresses. "It's so important to be aggressive with the follow-up, because HCC doubles at a rate of about every four to six months," adds Sherman. Ultrasound screenings can pick up tumors larger than 1 centimeter. A blood test reveals the level of the HCC tumor marker alpha-fetoprotein.

If the ultrasound detects a cancerous tumor, the next step is a CT scan or MRI to provide more information. When HCC is caught early, before reaching 6 centimeters, you're a candidate for a liver transplant, Sherman says. "But if the tumor is big, has spread outside the liver or has invaded important structures, then we don't have many options," says Luxon.

"Any patients with advanced fibrosis, F3 to F4, should be followed at six-month intervals with ultrasound and labs that assess their Model for End-Stage Liver Disease (MELD) score," Sherman says. The MELD score is calculated using a formula measuring bilirubin, creatinine and INR (prothrombin time). Changes indicate advancing liver disease. For instance, a spike in liver enzymes could signal reinfection with HCV.

Portal hypertension, high blood pressure in veins feeding into the liver, usually resolves after SVR. But if you have cirrhosis, you may still have esophageal varices, varicose veins in your esophagus that can rupture. Current guidelines recommend an initial upper endoscopy for a person with cirrhosis, says Luxon. "Then, depending on the size of the varices, every one to two years after that," he says.

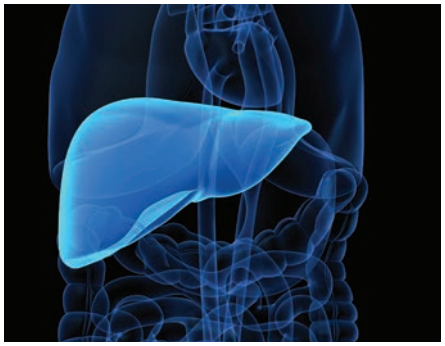
Patients with advanced liver disease need intermittent testing for antibodies to hepatitis A and B. "Those patients do not achieve as high a titer of antibody," says Sherman. They may need periodic booster shots, he adds.

HIV accelerates damage to the liver from HCV. This can lead to decompensation, in which the liver cannot repair itself. "If these patients have cirrhosis or F3 fibrosis, they need to be monitored for further decompensation and/or the development of liver cancer," Luxon says.

Don't disappear

Occasionally, a patient who failed to follow up has tragic consequences. "None of us likes to lose a patient whom we've treated," says Luxon.

Even though you've been cured of hepatitis C, you may still have liver damage, which could lead to liver disease and possibly liver cancer.



Eraxion/ThinkStock

Even though you've been cured of hepatitis C, you may still have liver disease. So don't ditch your doctor or stop scheduling important tests. "In some patients, we're doing the follow-up every six months for life," Sherman says. ●

Learn More

- Visit the American Liver Foundation website: liverfoundation.org
- Read the American Association for the Study of Liver Diseases/Infectious Diseases Society of America Hepatitis C Guidance: hcvguidelines.org
- Read MASAC recommendations on HCC: hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendations-on-Screening-for-Development-of-Hepatocellular-Cancer-in-Patients-with-Hepatitis-C

Six at a Time

New hep C drug cures major genotypes

BY SARAH M. ALDRIDGE, MS

Not one, not two, but all six of the most common genotypes, or genetic variants, of the hepatitis C virus (HCV) have a new foe: Epclusa®, manufactured by Gilead Sciences, Inc. The drug was approved by the Food and Drug Administration (FDA) on June 28 as the first all-oral drug to treat adults with chronic HCV infection from genotypes 1 to 6.

Epclusa contains 400 mg of sofosbuvir, a polymerase inhibitor that prevents HCV from reproducing, and 100 mg of velpatasvir, an NS5A inhibitor that prevents RNA replication and virus assembly. People with moderate to severe cirrhosis (liver scarring), which causes decompensation (the inability of the liver to repair itself), will need to take Epclusa with ribavirin.

Although there are several effective all-oral therapies to treat HCV genotype 1, found in 75% of Americans, until now there haven't been effective options for patients with the less common genotypes. Genotypes determine how well patients respond to treatment. According to Gilead, Epclusa is the first single-tablet regimen for treating patients with genotypes 2 and 3, found in 20% to 25% of Americans, without the need for ribavirin.

Trial run

Epclusa's safety and efficacy were tested in patients in a series of clinical studies called ASTRAL-1-4. During the phase 3 ASTRAL-1-3 trial, 1,035 subjects with chronic HCV infection were given Epclusa for 12 weeks. The patients had genotypes 1 to 6, but without cirrhosis or with compensated cirrhosis. Twelve weeks after treatment ended, 98% achieved sustained virologic response (SVR), meaning they were cured of HCV.

The ASTRAL-4 trial was conducted in patients with decompensated cirrhosis. One group was given Epclusa and ribavirin for 12 weeks; the second took Epclusa only for 12 weeks; the third took Epclusa only for 24 weeks. The groups achieved 94%, 83% and 86% SVR, respectively, 12 weeks after treatment had ended.

The most common adverse effects of Epclusa were headache and fatigue. Patients who also took ribavirin had additional adverse effects, such as nausea, diarrhea, anemia and insomnia. The FDA says the label will carry a warning that Epclusa can cause symptomatic bradycardia, a dangerous slowing of the heart's rhythm. Further, when taken with amiodarone, the combination has resulted in patients needing a pacemaker.

The FDA granted Epclusa its priority review, which speeds the approval process for a drug to treat serious health conditions. It also gave it a breakthrough therapy designation, awarded to a drug that has the potential to provide a major advancement in treatment over existing therapies.

"The approval of Epclusa represents an important step forward in the global effort to control and potentially eliminate HCV as it provides a safe, simple and effective cure for the majority of HCV-infected patients, regardless of genotype," said Ira Jacobson, MD, chairman of the Department of Medicine at Mount Sinai Beth Israel in New York, in a press release. He was a principal investigator in the clinical trials.

Like its previous direct-acting antiviral HCV drugs, Epclusa will have a steep price tag. Gilead estimates that a 12-week regimen will cost $74,760, or $890 per tablet. Patients who need assistance to pay for the drug can contact Gilead's Epclusa Co-pay Coupon Program. Call 855.769.7284 or go to: mysupportpath.com for more information on financial support. ●

Learn More

- Read the FDA press release on Epclusa: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm508915.htm

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YOU MIGHT WATCH THAT SHOW EVERYONE WATCHES

ELOCTATE is the first FVIII with a prolonged half-life and offers proven protection* from bleeds. It has a recommended starting prophylaxis infusion schedule of every 4 days. Talk to your healthcare provider about a schedule that could work for you.

*ELOCTATE has been proven to help patients prevent bleeding episodes using a prophylaxis regimen.

The recommended starting regimen is 50 IU/kg every 4 days as directed by your doctor. In children under 6 years of age, the recommended starting regimen is 50 IU/kg administered twice weekly. The regimen can be adjusted based on your body's individual response. Be sure to work with your healthcare provider to find a schedule that's right for you.

—Kenny, on ELOCTATE

Learn more at **ELOCATE.com/FourDays**

INDICATIONS AND IMPORTANT SAFETY INFORMATION

Indications
ELOCTATE is an injectable medicine that is used to help control and prevent bleeding in people with Hemophilia A (congenital Factor VIII deficiency). Your healthcare provider may give you ELOCTATE when you have surgery.

Important Safety Information
Do not use ELOCTATE if you have had an allergic reaction to it in the past.

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, are breastfeeding, are pregnant or planning to become pregnant, or have been told you have inhibitors (antibodies) to Factor VIII.

Allergic reactions may occur with ELOCTATE. 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 ELOCTATE, which may stop ELOCTATE from working properly.

The most frequently occurring side effects of ELOCTATE are headache, rash, joint pain, muscle pain and general discomfort. These are not all the possible side effects of ELOCTATE. Talk to your healthcare provider right away about any side effect that bothers you or that does not go away, and if bleeding is not controlled after using ELOCTATE.

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 back page for Brief Summary of full Prescribing Information. This information is not intended to replace discussions with your healthcare provider.

ELO-US-0949 04/16

FDA-Approved Patient Labeling
Patient Information
ELOCTATE®/el' ok' tate /
[Antihemophilic Factor (Recombinant), Fc Fusion Protein]

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

What is ELOCTATE?
ELOCTATE is an injectable medicine that is used to help control and prevent bleeding in people with Hemophilia A (congenital Factor VIII deficiency). Your healthcare provider may give you ELOCTATE when you have surgery.

Who should not use ELOCTATE?
You should not use ELOCTATE if you had an allergic reaction to it in the past.

What should I tell my healthcare provider before using ELOCTATE?
Talk to your healthcare provider about:
- Any medical problems that you have or had.
- All prescription and non-prescription medicines that you take, including over-the-counter medicines, supplements or herbal medicines.
- Pregnancy or if you are planning to become pregnant. It is not known if ELOCTATE may harm your unborn baby.
- Breastfeeding. It is not known if ELOCTATE passes into the milk and if it can harm your baby.

How should I use ELOCTATE?
You get ELOCTATE as an infusion into your vein. Your healthcare provider will instruct you on how to do infusions on your own, and may watch you give yourself the first dose of ELOCTATE.

Contact your healthcare provider right away if bleeding is not controlled after using ELOCTATE.

What are the possible side effects of ELOCTATE?
You can have an allergic reaction to ELOCTATE. Call your healthcare provider or emergency department 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 ELOCTATE. This can stop ELOCTATE from working properly. Your healthcare provider may give you blood tests to check for inhibitors.

Common side effects of ELOCTATE are headache, rash, joint pain, muscle pain and general discomfort. These are not the only possible side effects of ELOCTATE. Tell your healthcare provider about any side effect that bothers you or does not go away.

How should I store ELOCTATE?
- Keep ELOCTATE in its original package.
- Protect it from light.
- Do not freeze.
- Store refrigerated (2°C to 8°C or 36°F to 46°F) or at room temperature [not to exceed 30°C (86°F)], for up to six months.
- When storing at room temperature:
  - –Note on the carton the date on which the product is 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 ELOCTATE after the expiration date printed on the vial or, if you removed it from the refrigerator, after the date that was noted on the carton, whichever is earlier.

After reconstitution (mixing with the diluent):
- Do not use ELOCTATE if the reconstituted solution is not clear to slightly opalescent and colorless.
- Use reconstituted product as soon as possible.
- You may store reconstituted solution at room temperature, not to exceed 30°C (86°F), for up to three hours. Protect the reconstituted product from direct sunlight. Discard any product not used within three hours.

What else should I know about ELOCTATE?
Medicines are sometimes prescribed for purposes other than those listed here. Do not use ELOCTATE for a condition for which it was not prescribed. Do not share ELOCTATE with other people, even if they have the same symptoms that you have.

44279-02

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ELOCTATE®
[Antihemophilic Factor (Recombinant), Fc Fusion Protein]

Only on hemaware.org: Three strength-training moves you can do anywhere!

Trailblazer

Parcourses can spice up your workout

BY MATT MCMILLEN

If your walk, run or bike ride is becoming routine, try visiting a parcourse, or fitness trail, in your area. Developed in Switzerland in the late 1960s, parcourses feature exercise stations placed near a trail or bike path, or in a public park. Parcourses have been used as part of military fitness training, senior fitness programs and youth physical education. Now you can use them to spice up your workout.

A typical course has 10 to 20 stations, often constructed of steel or wood. Signs instruct you how to use equipment properly and indicate which muscles each station targets. Balance beams, pull-up bars and parallel bars are popular parcourse equipment. At first glance, the set-up may resemble your child's playground. But don't be fooled—this workout is for adults.

Parcourses are a good fit for people with bleeding disorders. "The equipment provided covers all the muscle groups," says Heidi Purrington, PT, a physical therapist at the Hemophilia and Thrombosis Center at Phoenix Children's Hospital in Arizona. "The trails are in public places, so they are free and easily accessible."

Tips before you try

Before you hit the circuit, check in with your physical therapist (PT). "Make sure that your joint health and your range of motion will allow you to do the individual exercises," says Nicole Hroma, PT, senior physical therapist at Lurie Children's Hospital in Chicago. "If your goal is to work your upper body, your PT can screen your shoulders, elbows and wrists." Your PT can also confirm that you're doing the exercises properly.

Some hemophilia treatment centers (HTCs) even offer similar exercise equipment, so you can practice as your PT observes and corrects your form. If your HTC doesn't have exercise equipment, you can take pictures of each station on your phone and send them to your PT to review.

"Know your limitations and plan which activities are best for you," advises Purrington. Your PT can also suggest ways to modify difficult exercises so that you can do them safely. Pushups, for instance, can be done standing up with your palms resting against a tree to ease stress on your arms and shoulders.

Start slowly. Warm up by walking and stretching for several minutes. Do the same after your workout to cool down. Focus on proper form rather than the number of repetitions. Increase the amount of exercise you do only after you are certain you are doing it right. "When you have good form, work up to doing 10 repetitions, or reps, at an easy pace before you add more reps," says Hroma.

Vary your focus. Exercise your leg muscles one day, then work your upper body the next time you are out. "Don't work your whole body all on one day," Hroma cautions. Limit yourself to three or four exercises each time you go. Plan to hit the parcourse two to three times a week.

A breath of fresh air

Parcourses allow you to escape the monotony of the gym in favor of the outdoors. To make your course even more fun and effective, invite a friend. "A partner's great for motivation and encouragement," says Purrington. Your friend can also check your technique, she says. "With guidance from your PT, you can make it work and have fun doing it," Purrington says. ●

Learn More

- Review safety recommendations for getting active: stepsforliving.hemophilia.org/sites/all/themes/stepsforliving/pdf/playing_it_safe.pdf
- Find a parcourse near you: myparcourse.com/parcourse/find-a-parcourse-near-you
- The Canadian Diabetes Association offers videos and tips for resistance band sessions: diabetes.ca/clinical-practice-education/professional-resources/resistance-exercise-videos

From Top: Leonardo Patrizi/Getty Images; Nancy Roy

The WFH Congress kicked off with a panel discussion featuring (left to right) Dennis da Costa, WFH President Alain Weill and Jorge de la Riva, chair, NHF Board of Directors.

Working Together

NHF contributes to successful WFH 2016 World Congress

BY VANESSA HERRICK, MANAGER, COMMUNICATIONS, WORLD FEDERATION OF HEMOPHILIA

This past July featured a first in the world of bleeding disorders: back-to-back meetings. First, the National Hemophilia Foundation's (NHF's) 68th Annual Meeting, then the World Federation of Hemophilia's (WFH's) World Congress. This unique opportunity gave US patients and their families the chance to participate in both of these key events to learn more about developments in bleeding disorders from a national and worldwide perspective.

The WFH 2016 World Congress was the best attended in history, with 5,482 participants from all around the world. The event featured the latest scientific developments, moving patient stories and a rich social program. Jens Bungardt, WFH Congress & meetings director, said planning and organizing the congress was a major endeavor that was greatly supported by NHF. "As an integral part of the Congress Organizing Committee, as well as the Medical and Multidisciplinary Program Committees, NHF was fully engaged and contributed at all stages to ensure attendees had a very special experience in Orlando," he says.

The WFH Congress would not have been possible without the generosity of a strong team of volunteers. This year, 80 of those volunteers were chapter staff from the Florida host chapters and NHF staff, who lent a helping hand to the WFH Congress right after the conclusion of NHF's 68th Annual Meeting on July 23. Another cornerstone of support came from those who helped organize and manage the treatment rooms both at the global national member organization (NMO) training during NHF's Annual Meeting and during WFH's World Congress. Specialized physicians, nurses and physical therapists

Continues on page 59

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Please see the Brief Summary of Prescribing Information on accompanying page.

Indications for COAGADEX

COAGADEX, a plasma-derived blood coagulation factor X concentrate, is indicated in adults and children (aged 12 years and above) with hereditary factor X deficiency for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding in patients with mild hereditary factor X deficiency

Perioperative management of bleeding in major surgery in patients with moderate and severe hereditary factor X deficiency has not been studied.

Important Safety Information for COAGADEX

COAGADEX is contraindicated in patients with known hypersensitivity to any of the components of the product.

Allergic type hypersensitivity reactions, including anaphylaxis, are possible with COAGADEX. If symptoms occur, patients should discontinue use of the product immediately and contact their physician.

The formation of neutralizing antibodies (inhibitors) to factor X is a possible complication in the management of individuals with factor X deficiency. Carefully monitor patients taking Coagadex for the development of inhibitors by appropriate clinical observations and laboratory tests.

COAGADEX is made from human plasma and may contain infectious agents, e.g. viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. No cases of transmission of viral diseases, vCJD or CJD, have been associated with the use of COAGADEX.

In clinical studies, the most common adverse reactions (frequency ≥5% of subjects) with COAGADEX were infusion site erythema, infusion site pain, fatigue and back pain.

Please refer to the Coagadex Prescribing Information for full prescribing details.

REFERENCE

1. COAGADEX® (Coagulation Factor X, Human) Prescribing Information. Durham, NC: BPL Limited. 2015.

March 2016 US/X/0316/0004

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For medical information queries, please call **1-866-398-0825** or email MedInfo@BPL-US.com

Coagadex HCP Brief Summary

The following is a brief summary only. See complete prescribing information on www.coagadex.com or request complete prescribing information by calling 1-866-398-0825.

INDICATIONS AND USAGE

COAGADEX, Coagulation Factor X (Human), is a plasma-derived human blood coagulation Factor indicated in adults and children (aged 12 years and above) with hereditary Factor X deficiency for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding in patients with mild hereditary Factor X deficiency.

Limitation of Use

Perioperative management of bleeding in major surgery in patients with moderate and severe hereditary Factor X deficiency has not been studied.

CONTRAINDICATIONS

COAGADEX is contraindicated in patients who have had life-threatening hypersensitivity reactions to COAGADEX or any of the components.

WARNINGS AND PRECAUTIONS

Hypersensitivity

Allergic type hypersensitivity reactions, including anaphylaxis, are possible. Early signs of hypersensitivity reactions including angioedema, infusion site inflammation (e.g. burning, stinging, erythema), chills, cough, dizziness, fever, flushing, generalized urticaria, headache, hives, hypotension, lethargy, musculoskeletal pains, nausea, pruritus, rash, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing. If hypersensitivity symptoms occur, discontinue use of the product immediately and administer appropriate emergency treatment.

COAGADEX contains traces of human proteins other than Factor X.

Neutralizing Antibodies

The formation of neutralizing antibodies (inhibitors) to Factor X may occur. Monitor all patients treated with COAGADEX for the development of inhibitors by appropriate clinical observations and laboratory tests. If expected Factor X activity levels are not attained, or if bleeding is not controlled with an expected dose, perform an assay that measures Factor X inhibitor concentration.

Transmissible Infectious Agents

Because COAGADEX is made from human blood, it may carry a risk of transmitting infectious agents, e.g. viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. There is also the possibility that unknown infectious agents may be present in the product. The risk that the product will transmit viruses has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and removing certain viruses during manufacture. Despite these measures, this product may still potentially transmit diseases.

All infections suspected by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare providers to BPL Inc. at 1-866-398-0825.

Monitoring and Laboratory Tests

- Monitor plasma Factor X activity by performing a validated test (e.g. one-stage clotting assay), to confirm that adequate Factor X levels have been achieved and maintained.
- Monitor for the development of Factor X inhibitors. Perform a Bethesda inhibitor assay if expected Factor X plasma levels are not attained, or if bleeding is not controlled with the expected dose of COAGADEX. Use Bethesda Units (BU) to report inhibitor levels.

ADVERSE REACTIONS

The most common adverse drug reactions (frequency ≥ 5% of subjects) observed in clinical trials were infusion site erythema, infusion site pain, fatigue, and back pain.

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 trial of another drug and may not reflect the rates observed in clinical practice.

During the clinical development of COAGADEX involving two multicenter, open-label, non-randomized clinical studies, 18 individual subjects with hereditary Factor X deficiency received at least one dose of COAGADEX.

Sixteen subjects aged 12 to 58 years with moderate to severe hereditary Factor X deficiency (basal FX:C < 5 IU/dL) received doses of COAGADEX for pharmacokinetic evaluation, on-demand treatment and control of bleeding episodes, and/or perioperative management of minor surgical or dental procedures. A total of 468 infusions were administered, including 242 for on-demand treatment and control of bleeding episodes, 6 for perioperative management and 31 for PK assessments. Spontaneous, traumatic and menorrhagic bleeding episodes were treated with a dose of 25 IU/kg for up to 2 years.

Two subjects aged 55 and 59 years with mild hereditary Factor X deficiency (basal FX:C 6 IU/dL and 8 IU/dL) received COAGADEX for perioperative management of four major surgical procedures. There were 40 exposure days to COAGADEX.

Immunogenicity

All subjects underwent Factor X inhibitor testing (inhibitor screen and Nijmegen-Bethesda assay) at baseline, end of study and at 3-monthly intervals in between. For subjects who underwent surgery, inhibitor testing was done pre-surgery and on discharge. All inhibitor tests were negative. Additionally, comparison of pharmacokinetic (PK) parameters at the repeat PK assessment with those at first dose did not suggest development of any inhibitors to Factor X.

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, it may be misleading to compare the incidence of antibodies to COAGADEX in the studies described above with the incidence of antibodies in other studies or to other products.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary: There are no data with COAGADEX use in pregnant women to inform on drug-associated risk. Animal reproduction studies have not been conducted using COAGADEX. It is not known whether COAGADEX can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. COAGADEX should be given to a pregnant woman only if clearly needed. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Lactation

Risk Summary: There is no information regarding the presence of COAGADEX in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COAGADEX and any potential adverse effects on the breast-fed infant from COAGADEX or from the underlying maternal condition.

Pediatric Use

Safety and effectiveness in patients under the age of 12 years have not been established.

Geriatric Use

Clinical studies of COAGADEX did not include any subjects aged 65 and over to determine whether they respond differently from younger subjects. Individualize dose selection for geriatric patients.

PATIENT COUNSELING INFORMATION

- Advise the patients to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
- Inform patients to immediately report the following early signs and symptoms of hypersensitivity reactions to their healthcare professional: angioedema, infusion site inflammation (e.g. burning, stinging, erythema), chills, cough, dizziness, fever, flushing, generalized urticaria, headache, hives, hypotension, lethargy, musculoskeletal pains, nausea, pruritus, rash, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing.
- Inform patients that the development of inhibitors to Factor X is a possible complication of treatment with COAGADEX. Advise the patients to contact their healthcare provider for further treatment and/or assessment if they experience a lack of clinical response to COAGADEX because this may be a manifestation of an inhibitor.
- Inform patients that COAGADEX is made from human plasma and may contain infectious agents that can cause diseases. While the risk that COAGADEX can transmit an infection has been reduced by screening plasma donors for prior exposure, testing donated plasma, and inactivating or removing certain viruses during manufacturing, patients should report any symptoms that concern them

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.

To report adverse events, or for additional information, call 1-866-398-0825.

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Continued from page 56

volunteered to assess emergency and semi-urgent situations related to bleeding disorders. They also assisted with infusions for patients who were not able to bring clotting factor concentrates to the US from their home countries.

NHF's close collaboration with the WFH was seen right from Day One of the congress, during the opening ceremony. The two bleeding disorders organizations worked together to develop a truly unique format for the event: a very personal panel discussion. NHF Chair of the Board Jorge de la Riva, WFH President Alain Weill, WFH CEO Alain Baumann and NHF CEO Val D. Bias all shared their personal stories and their common goal of supporting those with hemophilia. Many attendees said they found it encouraging knowing that the two bleeding disorders organizations were working together for the good of all patients and families coping with hemophilia and other bleeding disorders globally.

The 2016 WFH Congress featured a robust medical program with sessions on all of the important issues in today's world of bleeding disorders. Those included a look at the extended half-life factor products, innovations in immune tolerance induction for hemophilia and management of inhibitors. Topics also included gene therapy, genomic approaches to bleeding disorders and developments in the understanding of inhibitors.

Because NHF's Annual Meeting had no medical tracks this year, NHF, as the congress host, successfully applied for several medical educational grants that contributed directly to the World Congress program. The multidisciplinary program covered an equally large number of topics, such as patient care, new extended half-life products and women with hemophilia. It also included the impact of prophylaxis on children, an update on the effect of hepatitis C on patients with hemophilia and aging with hemophilia. Many of the events were eligible for continuing medical education or continuing education unit accreditation; NHF was instrumental in securing accreditation status for those sessions.

Jeanne White-Ginder became an AIDS advocate for awareness after her son, Ryan, died of HIV/AIDS from contaminated factor product to treat his hemophilia decades ago.

Topics also included gene therapy, genomic approaches to bleeding disorders and developments in the understanding of inhibitors.

Many patients and their families shared their stories and experiences during the congress. Jeanne White-Ginder shared her story of becoming a spokeswoman for people with AIDS after her teenage son, Ryan, died of AIDS after contracting HIV from contaminated factor product. Kari Atkinson talked about what it was like for her family when her son, Beau, was diagnosed with hemophilia and an inhibitor. And Gerard O'Reilly spoke of his experience with hemophilia and hepatitis C.

The social program was another highlight at the congress. One particular event stands out: the Host Country Networking Reception at the World Showplace Pavilion at Epcot. The evening featured great food, dancing and a totally unexpected visit by Mickey, Minnie, Donald, Pluto and Goofy. Not to mention the unforgettable grand finale of the IllumiNations: Reflections of Earth show.

The WFH 2016 World Congress was a resounding success. The WFH would like to thank all participants and sponsors for their support. A very special thank-you goes to NHF for collaborating with the WFH on many of the key elements that go into offering attendees a rewarding and unforgettable congress experience. ●

Learn More

- Find information about WFH's work and how you can help: wfh.org

Ties That Bond

Nurturing the needs of unaffected siblings

BY AMY LYNN SMITH

Cristina de la Riva, 23, has always been close to her younger brother, Jorge. In fact, she says they are best friends.

Jorge was diagnosed with severe hemophilia A at birth. His hemophilia immediately became a family affair. "When Jorge was diagnosed, our family was diagnosed," Cristina says. "We became a team that was going to figure this out together."

Although she was only 2 years old when Jorge was born, Cristina's parents told her the truth as soon as she was able to understand it. The family got involved right away with the Lone Star Chapter of the National Hemophilia Foundation (NHF) in Houston.

"When I was little, all I remember of hemophilia was my brother crying because he had a shot, so I related to hemophilia very negatively," Cristina says. "But later, as my mom became the director of the Lone Star Chapter, then I associated hemophilia with the community, going to bowl-a-thons, going to walks and doing fun stuff."

Cristina de la Riva (pictured above, with brother Jorge) credits her brother's hemophilia with making their family closer.

"Jorge only lets a few people experience his hemophilia with him, so I think it's made us closer," she says. "That's kind of a gift to the siblings in our community, something that is shared and can be a bonding experience within the family."

Open communication

For Cristina, being the unaffected sibling of someone with a bleeding disorder has been a positive experience overall. In fact, she appreciates the opportunities it has created, such as the chance to advocate and participate in NHF's National Youth Leadership Institute (NYLI), a three-year leadership training program for young adults ages 18 to 24.

But this is not always the case, according to Jeanne Safer, PhD, a psychotherapist and author of *The Normal One* (Delta, 2003). The title, she says, came from the unaffected siblings in families of children with disabilities or other challenges who self-identify as "the normal one" in the family.

According to Safer, it's important to let unaffected siblings talk about their frustrations and fears. "You can't make somebody feel certain things. You have to allow them to feel what they feel," she says. Parents should avoid telling unaffected siblings to "count your blessings" if they express negativity about their sibling's condition. "That squelches normal responses," says Safer.

Family members should avoid referring to the sibling with a bleeding disorder as having "special needs." After all, Safer says, all children have special needs of some sort. Consistently treating the sibling with a bleeding disorder as special can make unaffected siblings feel that they're not special or that their needs don't count.

Education, observation

Hiding the facts about bleeding disorders from unaffected siblings will only breed fear and uncertainty.

Cristina's parents let her be present for Jorge's clotting factor infusions, so she could see exactly what was involved. "I was in on it," she says. "Otherwise, it would have been this private thing between my father or mother and my brother. I would have felt left out. I would have seen hemophilia as an experience that was separate and foreign to my own."

What's more, Cristina's parents were candid with her about her risk of being a carrier of hemophilia, especially because her mother is a symptomatic carrier. Cristina was tested at age 19 and is not a carrier.

Let them shine

Safer points out that not all siblings will be naturally close. In fact, some aren't comfortable being part of their brother's or sister's care. She urges parents not to force camaraderie in these relationships. She also suggests spending some one-on-one time with unaffected siblings.

"Let them be the center of attention regularly," Safer says. "And let them have their own friends, activities and moments to shine."

"Your family bleeding disorder doesn't have to be something negative in your life. In our family, we became closer because of our bleeding disorder," says Cristina. ●

Learn More

- NHF's Steps for Living website offers information for siblings: https://stepsforliving.hemophilia.org/basics-of-bleeding-disorders
- Read how to help a child cope with a sibling's bleeding disorder in this *HemAware* article: hemaware.org/story/how-help-children-cope-their-siblings%E2%80%99-bleeding-disorder

HemAware Jr. for kids

When Your Brother or Sister Has a Bleeding Disorder

By Amy Lynn Smith
Illustration by John Haslam

If you have a brother or sister with a bleeding disorder, you probably have a lot of questions. You may wonder if you will get a bleeding disorder, too. If you have a small bruise or bleed and worry it might mean you have a bleeding disorder, ask your parents about it.

You may also wonder what it's like to have a bleeding disorder. Does your sister have a special doctor? Do those needles hurt? Maybe you worry about what games are safe to play with your brother or sister.

The more you know about your sibling's bleeding disorder, the less you will feel afraid or anxious.

Here are some other ideas that may help you and your family:

- **Learn more**. Find out about your sibling's treatment. Or just be there when your brother or sister wants to talk about it.
- **Share your feelings**. Talk to your parents if you're scared or if you feel like you don't get much attention. Those feelings are normal. Usually it feels better to share your feelings with others than to bottle them up inside.
- **Do things you enjoy**. Your parents may encourage you to do things with your brother or sister, as long as they're safe. But it's also OK to want to do things your sibling can't, like play basketball or ice skate. Talk to your mom or dad about trying a new hobby or sport—just for you.

At times, your brother or sister will need extra attention. Sometimes it may even seem as if your sibling gets all the attention. But remember that your parents are doing their best to love and support everyone in your family, including *you*.

For more articles and fun facts, go to: hemaware.org/junior.

Knowing and Doing

NHF's website targets undiagnosed, untreated women

BY EMILY ROGAN

For women with bleeding disorders, a diagnosis can be life-changing. But once they have a healthcare team and a treatment plan, they can live healthier, less stressful and more productive lives.

Unfortunately, many women living with bleeding disorders remain undiagnosed. They have the characteristic signs of a bleeding disorder—heavy and painful periods, bruising and anemia. What they lack is the relief in knowing the cause and how it can be treated.

"We hear over and over again about women who are living with bleeding disorders and don't know it," says Corinne Koenig, MS, manager of education and training for the National Hemophilia Foundation (NHF).

Betteryouknow.org

NHF's latest site, betteryouknow.org, is one way to reach outside of the bleeding disorders community to advance awareness and education among undiagnosed people. One part of the site will be directed to men and another, specifically to women.

Betteryouknow.org is easy to use. It's packed with important information and valuable resources. In short YouTube videos, women speak candidly about personal experiences with bleeding disorders. Topics include how long it took to be diagnosed, family history, intimacy and day-to-day living.

First steps to treatment

The ultimate objective of betteryouknow.org is to help women seek proper diagnosis, treatment and care for their symptoms, explains Kate Nammacher, MPH, NHF director of education. Women click the "I Want to Know" assessment tool and answer several questions. The site then directs them to information in a question-and-answer format that explains what to do next.

"The real work is to go and talk to that first provider who may be able to give them a diagnosis or refer them to a hematologist," says Nammacher. "There are potentially many steps for these women, so we wanted to keep it a simple, clear action plan."

"We want women out there in the world who are living with bleeding disorders and don't know it to get a diagnosis and treatment."

The site also provides checklists, bleeding logs and other documents to help women self-assess and seek additional care. Women who take the screening tool and do not meet the criteria for bleeding disorders are also provided with links to other women's health resources.

Women helping women

This new site also empowers women already diagnosed with bleeding disorders, enabling them to do more than just share their stories. "It's giving women in our community more options to help other women deal with their symptoms and get treatment in a tangible, easy way," Nammacher says. Women can send a friend a video, questions to ask a doctor or a menstrual period tracking chart.

Spreading the word

The website is one part of a broader information campaign, the result of a five-year grant from the Centers for Disease Control and Prevention (CDC), says Koenig. This greater initiative will create partnerships with companies, nonprofits and colleges across the country, reaching more women and directing them to the website.

Future plans include live webinars targeting healthcare providers not familiar with bleeding disorders. These education courses will teach doctors and nurses about bleeding disorders. When women come in and present with symptoms, their healthcare providers will be better informed.

Postcards with a checklist of symptoms, general information about bleeding disorders, and the

iStock

When It Comes to Your Body, You're the Expert

If you suspect you have a bleeding disorder, you can take charge of your healthcare. Corinne Koenig, MS, National Hemophilia Foundation (NHF) manager of education and training, suggests these three steps:

- **Educate yourself. Visit betteryouknow.org.** Take the assessment tool. Read the associated links. Find out more about bleeding disorders in general. Familiarize yourself with the process of diagnosis.
- **Keep track of your menstrual bleeding.** Be specific in terms of how many pads or tampons you use. Betteryouknow.org has a bleeding diary that makes it easy to track each day of your period. Bring the diary to your doctor as evidence that your periods are abnormal.
- **Contact your local NHF chapter.** You'll find camaraderie, information and support. Go to: hemophilia.org to find the chapter nearest you.

Better You Know logo and website address will be available at doctors' offices. Local NHF chapters will receive Better You Know toolkits to help them communicate with women.

"We want women out there in the world who are living with bleeding disorders and don't know it to get a diagnosis and treatment," says Koenig. "We want them to improve their quality of life." ●

Learn More

- Take the assessment: betteryouknow.org
- Read articles for women with bleeding disorders: hemaware.org/women
- Review resources and find a local hemophilia treatment center: hemophilia.org
- Get more information about von Willebrand disease: cdc.gov/ncbddd/vwd

Coming in Winter 2017

▶ **Dads and Daughters**
Real-life stories of self-discovery and advocacy.

▶ **Infusion ABCs**
Managing infusion stress, with tips for parents and children.

ThinkStock

ADVERTISER INDEX

NHF's Connections for Learning grant recipients enjoy the Annual Meeting experience, many for the first time.

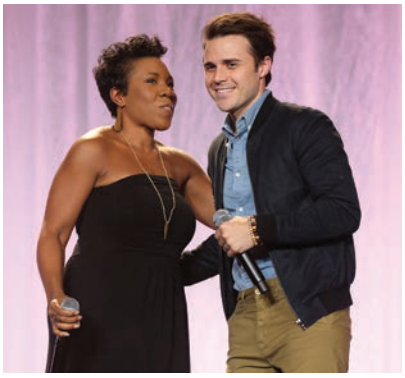
Annual Meeting At a Glance

Education, inspiration and entertainment mark the 2016 gathering in Florida

Universal Studios Orlando was the place to be for the Final Night Event.

Clear blue skies and bright sunlight greeted the more than 2,700 attendees who gathered in Orlando, Florida, on July 21–23 for the 68th Annual Meeting of the National Hemophilia Foundation (NHF). It was a chance for people from across the country to get together to gain valuable education, reconnect with old friends and make new ones, and learn about the latest bleeding disorders treatments in the pipeline. But this year, there were even more faces in the crowd, as the Annual Meeting ran concurrently with the World Federation of Hemophilia's (WFH's) global member organization training, giving the NHF meeting a decidedly international flavor.

NHF's Annual Meeting officially kicked off with NHF CEO Val D. Bias welcoming this international audience. The inspiring speech emphasized NHF's continuing commitment to improving the lives of people with bleeding disorders in the US through research and access to care, and around the world through support for WFH's international aid programs.



American Idol contestants Melinda Doolittle and Kris Allen shared the stage and a song during the Opening Session.

A diverse array of educational sessions offered attendees knowledge on a variety of topics. For families, The Comprehensive Care Show provided an interactive look at a visit to

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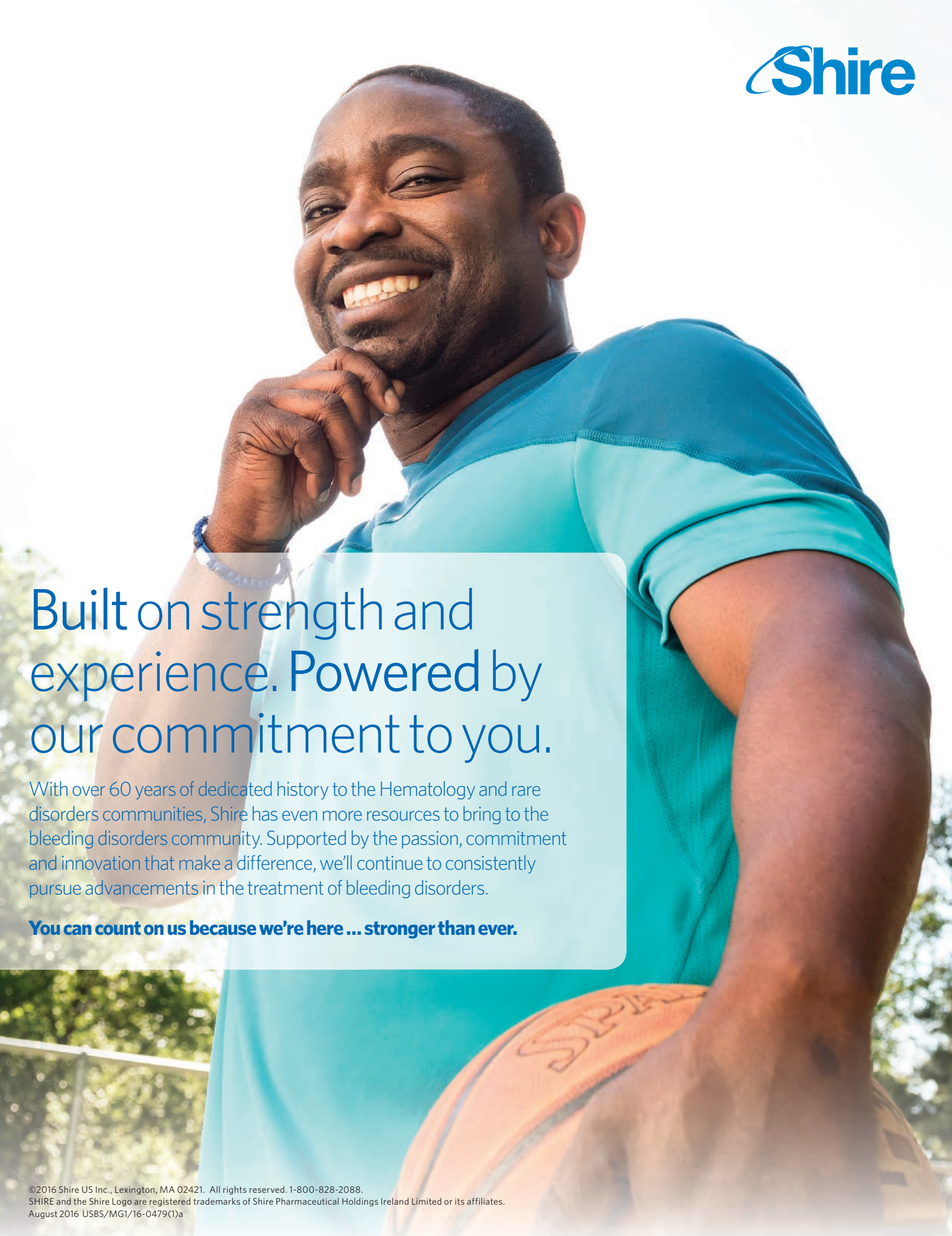


The Exhibit Hall's interactive displays appealed to children and adults alike.

Fathers and daughters took the stage to share their experiences.

Continued from page 64

a hemophilia treatment center. There were also sessions on reducing stress at infusion time and managing pain in children. Consumers learned how to partner with healthcare providers to ensure better care and information on new treatments, blood safety and insurance issues.

For people affected by von Willebrand disease (VWD), NHF provided a four-hour preconference. It included an Ask the Expert session and additional sessions on new and emerging treatments and joint health.

NHF underlined the importance of staying active with five Healthy Steps sessions. Attendees could get their blood pumping with Just Dance, kick off a healthy morning with the Fit and Fun Walk/Run, or recharge their minds and bodies with yoga or tai chi.

Sessions for women with bleeding disorders offered something for women at every stage in their lives. They included an in-depth discussion of hormone therapy, a session on pregnancy and childbirth, and a session on aging gracefully with a bleeding disorder.

No matter the age, everybody learns when generations compare notes.

The Teen Track provided many opportunities for collaboration and problem-solving skills.

Healthy Steps: Let's Dance got attendees into the groove.

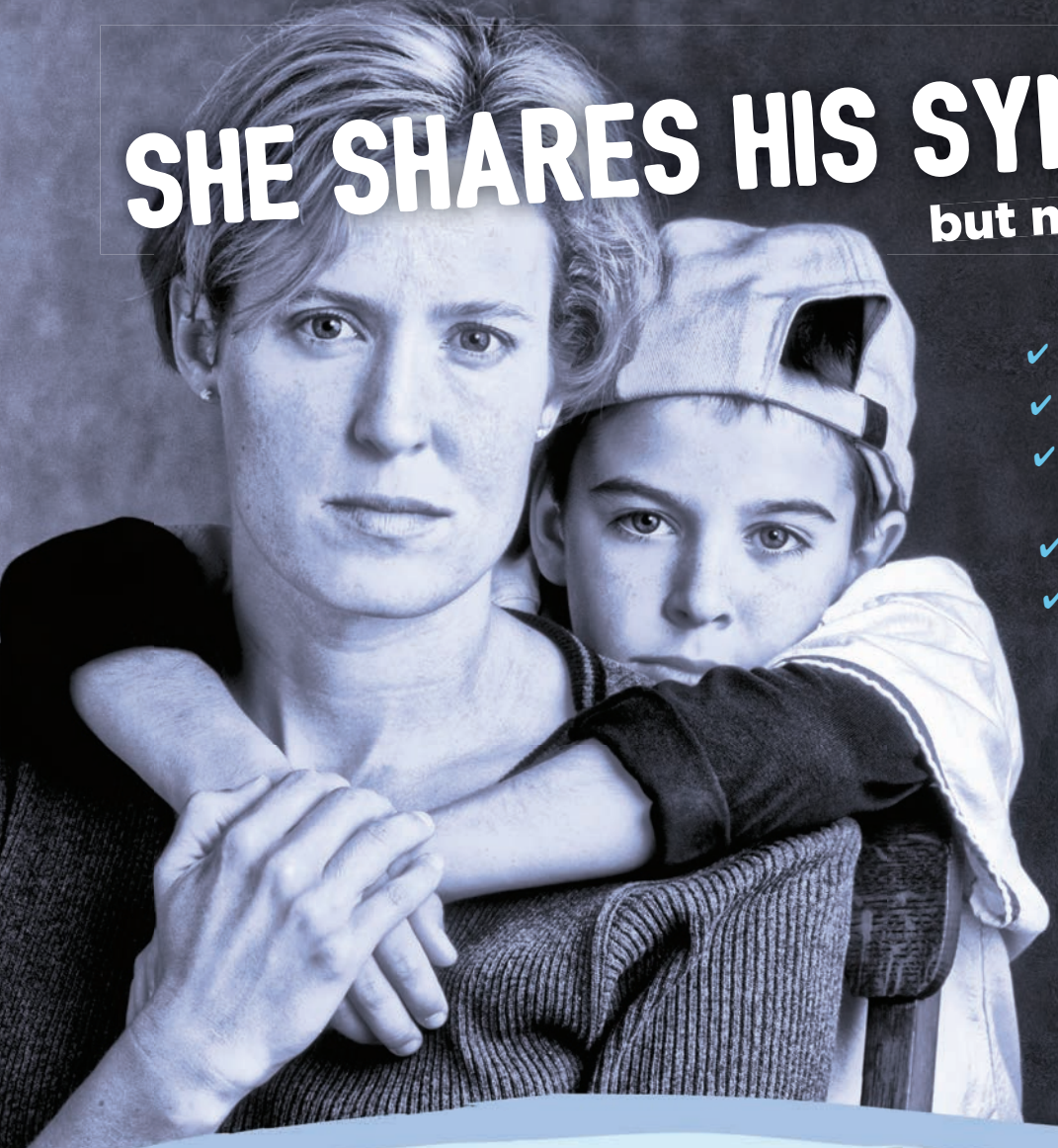
Adult men with bleeding disorders learned tips on planning for retirement as well as options for long-term care. Similarly, partners and spouses had sessions that focused on building strong partnerships and how to fit into the community when you aren't affected by a bleeding disorder.

The meeting closed with NHF's Final Night Event at Universal Studios Orlando, where attendees could visit Harry Potter's Diagon Alley or take a 3-D adventure with minions.

NHF is grateful to platinum sponsors Baxalta (now part of Shire), Bayer, Biogen, CSL Behring, Novo Nordisk and Pfizer, and silver sponsor Octapharma.

Don't forget to mark your calendars for next year: NHF's 69th Annual Meeting will take place August 24–26, 2107, in Chicago. We'll see you there! ●

SHE SHARES HIS SYMPTOMS, but not his solutions.



- ✔ Below-normal factor IX levels
- ✔ Chronic pain
- ✔ Prolonged bleeding after dental work or surgery
- ✔ Easy bruising
- ✔ Joint damage from bleeding

> **I knew I was a carrier, and I was having symptoms for years, but I wasn't diagnosed until the age of 36.**
>
> *— 46-year-old woman with hemophilia B*

Women and girls can—and do—have hemophilia B.

Traditionally classified as carriers, women can have the same bleeding symptoms as men with hemophilia B.

They also face challenges all their own, like abnormally heavy and long menstrual cycles with large blood clots, excessive bleeding after giving birth, and anemia.[1-3]

Don't let the wrong diagnosis be one of those challenges.

Early diagnosis and the right treatment can help or even prevent bleeding problems and improve quality of life.[2]

That's why Aptevo Therapeutics worked with women who have hemophilia B to create a quick guide that focuses on how this condition affects women, girls, and their families.

With help from this guide, you can feel confident talking about your symptoms with your doctor or nurse.

Download a women's guide to hemophilia B at **WomenWithHemophiliaB.com**

References: 1. Clark D. Women with hemophilia. Coalition for Hemophilia B. Available at http://static1.squarespace.com/static/566b210340667a1cc1623840/t/56792e35a2bab8836bd402dc/1450782261872/Women-with-Hemophilia.pdf Accessed June 28, 2016. **2.** Rhynders PA, Sayers CA, Presley RJ, Thierry JM. Providing young women with credible health information about bleeding disorders. *Am J Prev Med.* 2014;47(5):674-680. **3.** Hemophilia Federation of America. Are women affected by bleeding disorders? Available at: http://www.hemophiliafed.org/bleeding-disorders/can-women-have-bleeding-disorders. Accessed August 5, 2016.

Aptevo™ Therapeutics

Taking the Cake

Bringing smiles to kids who are ill

BY BETH MARSHALL

In each issue of *HemAware*, we spotlight someone in the bleeding disorders community. In this issue, we speak with Daniela Delgado, 9, from Stamford, Connecticut, with severe von Willebrand disease (VWD), type 1 C. Along with her parents, Janine Achury and Nemorio Delgado, she created Daniela's Little Wish, which delivers cakes to children with disabilities or illnesses.

How did you first discover your love of baking?

Ever since I can remember, everyone in my home was baking. My parents are both cake designers. When my grandma comes to visit she is always baking. I guess it just runs in the family. My home always smells delicious because there is always a cake in the oven!

How did your cake baking turn into a charity to help others?

I had a friend in pre-K named Kevin who had cerebral palsy. I used to try and help him because he couldn't do a lot of the activities we did. I wanted to try and help more kids, but I couldn't figure out how until I thought of cake! I just want to bring a smile to kids' faces, and help them forget their illnesses. So now people find us on Facebook or through word of mouth, and tell us what kind of cake they want. We give them a cake for free for their birthday.

How does VWD affect your life?

I have a lot of nosebleeds, sometimes during the middle of the night or during the day. Sometimes I can't play certain contact sports because I don't want to get hit, so I have to sit out PE to avoid the other kids playing rough. I have a special medication to help me stop the bleeding. When I was 8 years old, I learned to infuse myself with factor. I practice how to do it, just in case I have an emergency or a heavy bleed. I know it looks scary to some people, but it actually makes me happy that I know how to do it.

Daniela Delgado delivers cakes and smiles to kids.

You can find Daniela's Little Wish on Facebook, Pinterest, YouTube and Twitter.

Facebook
www.facebook.com/danielaslittlewish

Twitter
@danilittlewish

Instagram
www.instagram.com/danielaslittlewish

Pinterest
www.pinterest.com/danielaslittlew

What do you want people who don't have a bleeding disorder to know?

Bleeding disorders aren't contagious, and are actually passed on from generation to generation. I want people to know that bleeders are not to be bullied. I talk about my bleeding disorder with my friends and family because I want them to know not only about my condition, but also if they have symptoms that they should get them checked out.

At 9, you've already done a lot with your life. What do you want to do in the future?

I want kids who have a special condition to know that we need to love ourselves as we are. I would like all people to accept and love all kids with illnesses or disabilities because even though we have differences, we're really all the same.

I want to continue giving cakes to children with illnesses and disabilities. The more smiles I bake, the better. I want Daniela's Little Wish to grow and bring cakes not only to kids in Connecticut, but also to kids across the US. And why not the world? I know those are big dreams, but with my mom and dad to support me, I think I can do it! ●

Do you know an interesting individual who would like to be profiled in *HemAware*? E-mail: libby.hawkins@manifest.com.

IDELVION®, Coagulation Factor IX (Recombinant), Albumin Fusion Protein
Initial U.S. Approval: 2016

BRIEF SUMMARY OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use IDELVION safely and effectively. Please see full prescribing information for IDELVION, which has a section with information directed specifically to patients.

What is IDELVION?

IDELVION is an injectable medicine used to replace clotting Factor IX that is absent or insufficient in people with hemophilia B. Hemophilia B, also called congenital Factor IX deficiency or Christmas disease, is an inherited bleeding disorder that prevents blood from clotting normally.

IDELVION is used to control and prevent bleeding episodes. Your healthcare provider may give you IDELVION when you have surgery. IDELVION can reduce the number of bleeding episodes when used regularly (prophylaxis).

Who should not use IDELVION?

You should not use IDELVION if you have had life-threatening hypersensitivity reactions to IDELVION or are allergic to:

- hamster proteins
- any ingredients in IDELVION

Tell your healthcare provider if you have had an allergic reaction to any Factor IX product prior to using IDELVION.

What should I tell my healthcare provider before using IDELVION?

Discuss the following with your healthcare provider:

- Your general health, including any medical condition you have or have had, including pregnancy, and any medical problems you may be having
- Any medicines you are taking, both prescription and non-prescription, and including any vitamins, supplements, or herbal remedies
- Allergies you might have, including allergies to hamster proteins
- Known inhibitors to Factor IX that you've experienced or been told you have (because IDELVION might not work for you)

What must I know about administering IDELVION?

- IDELVION is administered intravenously, directly into the bloodstream.
- IDELVION can be self-administered or administered by a caregiver with training and approval from your healthcare provider or hemophilia treatment center. **(For directions on reconstituting and administering IDELVION, see the Instructions for Use in the FDA-Approved Patient Labeling section of the full prescribing information.)**
- Your healthcare provider will tell you how much IDELVION to use based on your weight, the severity of your hemophilia B, your age, and other factors. Call your healthcare provider right away if your bleeding does not stop after taking IDELVION.
- Blood tests may be needed after you start IDELVION to ensure that your blood level of Factor IX is high enough to properly clot your blood.

What are the possible side effects of IDELVION?

Allergic reactions can occur with IDELVION. Call your healthcare provider right away and stop treatment if you get a rash or hives, itching, tightness of the chest or throat, difficulty breathing, light-headedness, dizziness, nausea, or decrease in blood pressure.

Your body can make antibodies, called inhibitors, against Factor IX, which could stop IDELVION from working properly. Your healthcare provider may need to test your blood for inhibitors from time to time.

IDELVION might increase the risk of abnormal blood clots forming in your body, especially if you have risk factors for such clots. Call your healthcare provider if you experience chest pain, difficulty breathing, or leg tenderness or swelling while being treated with IDELVION.

A common side effect of IDELVION is headache. This is not the only side effect possible. Tell your healthcare provider about any side effect that bothers you or does not go away.

Please see full prescribing information, including FDA-approved patient labeling.

IDELVION®
Coagulation Factor IX (Recombinant), Albumin Fusion Protein

IDELVION®
Coagulation Factor IX (Recombinant), Albumin Fusion Protein

He's free to infuse only once every 14 days. **Are you?**

The only FDA-approved treatment for hemophilia B with up to 14-day dosing.* **Visit us at IDELVION.com.**

UP TO 14-DAY DOSING*
Dosing schedule that fits into your lifestyle

ABOVE 5% FOR 14 DAYS AT HIGHEST DOSE
High and sustained Factor IX levels

ZERO BLEEDS MEDIAN ASBR
A median annualized spontaneous bleeding rate of zero in 7- and 14-day prophylaxis

*In appropriate people 12 years and older. Talk with your doctor.

Important Safety Information

IDELVION is used to control and prevent bleeding episodes in people with hemophilia B. Your doctor might also give you IDELVION before surgical procedures. Used regularly as prophylaxis, IDELVION can reduce number of bleeding episodes.

IDELVION is administered by intravenous injection into the bloodstream, and can be self-administered or administered by a caregiver. Do not inject IDELVION without training and approval from your healthcare provider or hemophilia treatment center.

Tell your healthcare provider of any medical condition you might have, including allergies and pregnancy, as well as all medications you are taking. Do not use IDELVION if you know you are allergic to any of its ingredients, including hamster proteins. Tell your doctor if you previously had an allergic reaction to any FIX product.

Stop treatment and immediately contact your healthcare provider if you see signs of an allergic reaction, including a rash or hives, itching, tightness of chest or throat, difficulty breathing, lightheadedness, dizziness, nausea, or a decrease in blood pressure.

Your body can make antibodies, called inhibitors, against Factor IX, which could stop IDELVION from working properly. You might need to be tested for inhibitors from time to time. IDELVION might also increase the risk of abnormal blood clots in your body, especially if you have risk factors. Call your healthcare provider if you have chest pain, difficulty breathing, or leg tenderness or swelling.

In clinical trials for IDELVION, headache was the only side effect occurring in more than 1% of patients (1.8%), but is not the only side effect possible. Tell your healthcare provider about any side effect that bothers you or does not go away, or if bleeding is not controlled with IDELVION.

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 prescribing information for IDELVION on previous page.