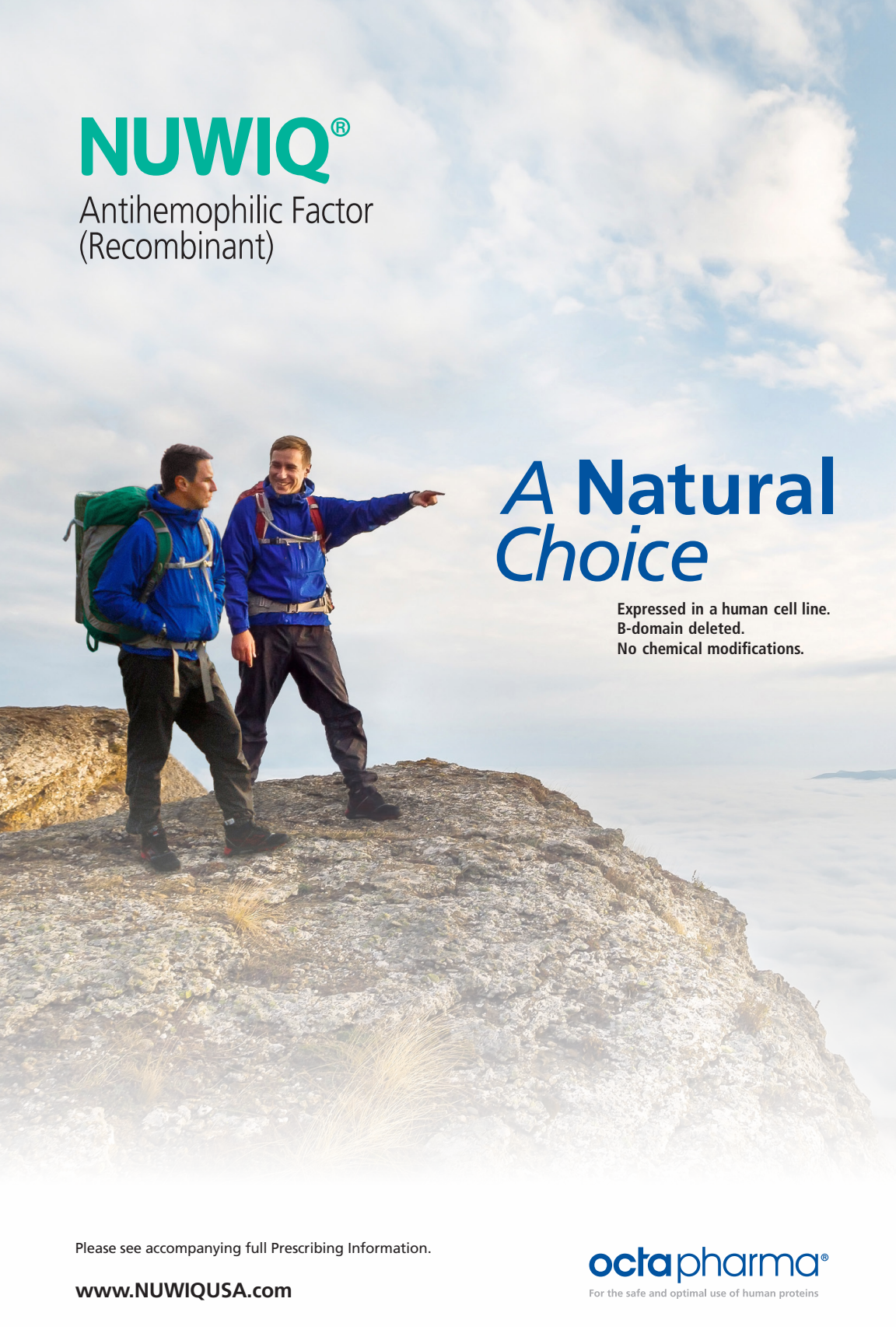
NUWIQ®

Antihemophilic Factor
(Recombinant)



A **Natural** *Choice*

Expressed in a human cell line.
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No chemical modifications.

Please see accompanying full Prescribing Information.

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octapharma®
For the safe and optimal use of human proteins

FACTOR VIII REPLACEMENT: THE FOUNDATION OF HEMOPHILIA TREATMENT

Hemophilia A is an inherited bleeding disorder that results from a deficiency of coagulation Factor VIII (FVIII).[1] It's only natural then, that the management of Hemophilia A is generally based on the replacement of the missing FVIII.

In the 1950s and early 1960s, the only treatment options for people with Hemophilia A were transfusions of whole blood or fresh frozen plasma transfused in the hospital. These transfusions contained the naturally occurring FVIII from people who didn't have Hemophilia. By the 1970s, freeze-dried powdered FVIII concentrates became available. These factor concentrates could be stored at home. This allowed patients to self-infuse at home and avoid trips to the hospital.

ADVANCING HEMOPHILIA TREATMENT

A new era in the management of Hemophilia A began in 1984 when the FVIII gene was first cloned.[1] This would lead to one of the greatest advances in Hemophilia management—the first genetically engineered FVIII molecules produced in hamster cell lines.[1] These products, called recombinant FVIII (rFVIII), would become the mainstay of Hemophilia treatment for the next 20 years.

In 2015, Octapharma introduced a new treatment for Hemophilia A—NUWIQ, a rFVIII product that is produced using human cells, not hamster cells. Because NUWIQ production cells are human, the protein produced closely resembles the FVIII that is produced naturally in the human body.[2,3]

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.

FACTOR VIII IS THE STANDARD OF CARE

FVIII replacement therapy is the standard of care for Hemophilia A.[1] FVIII replacement is a trusted therapy that has been proven to be safe and effective over decades of use.

The way that FVIII works in the body is well understood by the doctors and nurses who prescribe it. And measuring FVIII levels with routine laboratory testing has helped make replacement therapy with FVIII the standard of care for Hemophilia.

Important Safety Information

NUWIQ® is contraindicated in patients who have manifested life-threatening hypersensitivity reactions, including anaphylaxis, to the product or its components. The formation of neutralizing antibodies (inhibitors) to Factor VIII can occur following the administration of NUWIQ.

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HAVE YOU BEEN THINKING ABOUT SWITCHING YOUR HEMOPHILIA A TREATMENT?

Today, many treatment choices are available, so you might be thinking about switching your Hemophilia A treatment. Working together with your physician to choose a product that's right for you is one of the biggest decisions you'll ever make. So, be sure to take the time to do your homework and choose carefully. The questions in this brochure are designed to help identify some of the issues you might want to consider in your decision-making process.

HOW WELL DO YOU **REALLY** KNOW THE TREATMENT YOU'RE CURRENTLY USING?

There are lots of things you should know about your current treatment. For example:

- How does your treatment work?
- How safe is it?
- How well did it perform in clinical studies?

Check out the product information and key facts about your current treatment. Things like how the product is made, the annual bleeding rate (ABR), and its safety record are very important considerations.

WHAT MATTERS MOST TO YOU IN CHOOSING YOUR HEMOPHILIA A TREATMENT?

Think about the things that may matter most to you in choosing a treatment for your Hemophilia. Consider the following:

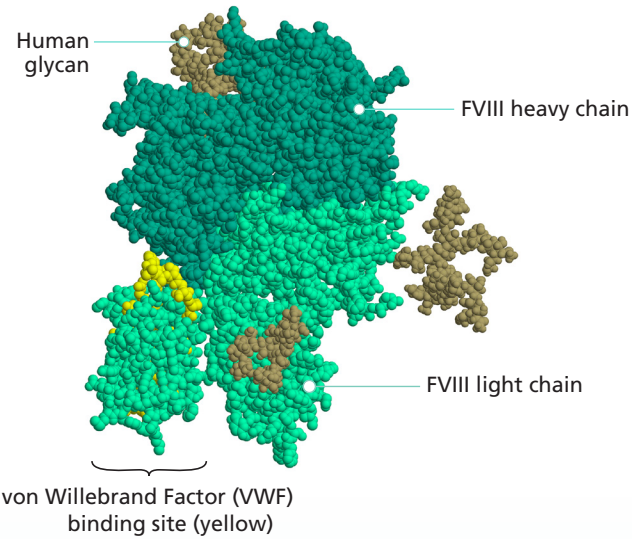
- The source of cells used to make the product. Is it made from animal cells or human cells?
- Effective bleeding control. What is the ABR?
- Safety concerns. Are you worried about inhibitors if you switch your FVIII treatment? (Current evidence shows that switching FVIII products in previously treated patients [PTPs] carries minimal risk for inhibitor development[4])
- Convenience. How important is dosing flexibility?

CONSIDER NUWIQ—*A* NATURAL *CHOICE*

NUWIQ is a rFVIII treatment produced using human cells, not hamster cells. In fact, no animal or human proteins are added during the manufacturing of NUWIQ.[2,3]

In addition:

- NUWIQ was shown to be effective in controlling bleeding[5]
- NUWIQ was not associated with the development of antibodies, also known as inhibitors, in studies with PTPs who switched to NUWIQ[5]
- NUWIQ was shown to be safe in previously untreated patients (PUPs)[6]
- NUWIQ has the potential to extend your dosing interval with personalized prophylaxis[7]
- NUWIQ is available in a wide range of dosage strengths for individual dosing needs



Important Safety Information

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.

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BLEEDING CONTROL WITH NUWIQ

HOW WELL DOES YOUR CURRENT rFVIII PRODUCT CONTROL YOUR BLEEDING?

NUWIQ was proven to control bleeding in adults and children[5]

Prophylaxis treatment with NUWIQ was shown in studies to be effective for reducing the frequency of bleeding episodes in adults and children with severe Hemophilia A.

in a study with 32 adults treated with prophylaxis for 6 months or more[5]

- Median ABR for all bleeds was **0.9**

in a study with 59 children treated with prophylaxis for 6 months or more[5]

- Median ABR for all bleeds was **1.9**

Important Safety Information

NUWIQ® is contraindicated in patients who have manifested life-threatening hypersensitivity reactions, including anaphylaxis, to the product or its components. The formation of neutralizing antibodies (inhibitors) to Factor VIII can occur following the administration of NUWIQ.

WHAT MAKES NUWIQ DIFFERENT FROM rFVIII PRODUCTS MADE FROM HAMSTER CELL LINES?

DID YOU KNOW THAT MANY rFVIII PRODUCTS, AND SOME NONFACTOR PRODUCTS, ARE MADE FROM HAMSTER CELL LINES?

NUWIQ is a rFVIII produced in a human cell line

NUWIQ is not made from hamster cells, but from human cells. Because NUWIQ is produced in human cells and more closely resembles natural, human FVIII, the immune system may be less likely to see it as foreign and make antibodies against it.[2]

NUWIQ binds strongly to VWF

NUWIQ has been shown to bind strongly to VWF, another coagulation factor.[2] VWF has a naturally long half-life. This means that it stays in the body for a long time and is available to help the blood clot when it's needed. FVIII can benefit from this long half-life if it binds strongly to VWF.[8] The longer the FVIII can remain in the body, the longer it can be available to help the blood to clot.

Studies that were done to measure the mean (average) half-life of NUWIQ showed the following[5]:

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ARE YOU CONCERNED ABOUT THE POSSIBILITY OF DEVELOPING FVIII INHIBITORS IF YOU SWITCH PRODUCTS?

Current evidence shows that switching FVIII products in PTPs carries minimal risk for inhibitor development. Among patients who have been previously treated with FVIII (>150 exposures), inhibitor risk from switching to a new product is less than 1%.[4]

NUWIQ was not associated with the development of inhibitors in studies with PTPs

In studies that included 135 patients who had previously been treated with other FVIII products, none of the patients treated with NUWIQ developed inhibitors.[5]

INTERIM RESULTS FROM THE ONGOING *NuPROTECT* STUDY

The safety and efficacy of NUWIQ in PUPs with severe Hemophilia A is currently being studied in a trial called *NuProtect*. The trial is evaluating 110 PUPs, making *NuProtect* the largest prospective study ever done with a single FVIII product. In an early, or interim, analysis from *NuProtect*, data from 66 PUPs treated with NUWIQ for at least 20 exposure days were evaluated. **These interim data showed a 12.8% incidence of high-titer inhibitors.**[6]*

12.8% in PUPs treated with NUWIQ

The incidence of inhibitors with rFVIII products made in hamster cells

A recent study, the **Survey of Inhibitors in Plasma-Product Exposed Toddlers**, or **SIPPET**, compared the rates of inhibitors in PUPs. Patients in the study had severe Hemophilia A and were treated with either plasma-derived (nonrecombinant) FVIII (pdFVIII) or rFVIII made from hamster cells. Patients were followed in the study for 50 consecutive days of exposure to the FVIII products, or 3 years, or until it was confirmed that inhibitors had developed.[9]

Results from the SIPPET study showed that PUPs treated with rFVIII products from hamster cells had a higher incidence of inhibitor development than PUPs who had been treated with pdFVIII.[9†]

28.4% in PUPs treated with rFVIII from hamster cells

18.6% in PUPs treated with pdFVIII

*Results are from an interim analysis of the *NuProtect* study and do not reflect final study results. Information from the *NuProtect* study is presented in parallel to the SIPPET study for context, but please note that these trials were performed under different conditions and with different populations. These data have not been presented to the FDA for evaluation.

† Differences in high-titer inhibitor rates between pdFVIII and rFVIII were not found to be statistically significant. SIPPET authors suggested this may have been due to the small sample size of the study.

SAFETY WITH NUWIQ

HOW SAFE IS YOUR CURRENT TREATMENT? WERE THERE ANY SERIOUS ADVERSE REACTIONS DURING CLINICAL STUDIES?

NUWIQ was shown to be safe in clinical studies that included 135 PTPs.[5]

In these studies:

- No patients experienced serious adverse reactions to NUWIQ
- No patients experienced anaphylaxis, a very serious allergic reaction
- No patients dropped out of the study because of an adverse reaction to NUWIQ
- No deaths were reported

Important Safety Information

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.

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DOSING FLEXIBILITY WITH NUWIQ

ARE YOU INTERESTED IN THE POSSIBILITY OF FEWER WEEKLY INFUSIONS?

Everyone knows how important convenience is. But it's also important to not sacrifice bleeding control for convenience. The *NuPreviq* trial confirmed that personalized prophylaxis with NUWIQ is effective. Patients in the study were PTPs with severe Hemophilia A. The majority of these patients achieved **twice-weekly infusions while maintaining bleeding control.**[7]

DOES YOUR CURRENT TREATMENT OFFER A WIDE RANGE OF DOSAGE STRENGTHS?

NUWIQ offers a broad range of vials with the lowest, 2.5 mL diluent volume

NUWIQ is available in 250 IU, 500 IU, 1000 IU, 2000 IU, 2500 IU, 3000 IU, and 4000 IU vials. Larger single-dose vials of 2500, 3000, and 4000 IU offer greater flexibility and convenience for patients requiring larger doses of FVIII.

Having more vial options allows for simple dosing. For example, a patient who requires 2500 IU can use one 2500 IU vial instead of having to use a 2000 IU vial and a 500 IU vial.

250 IU | 500 IU | 1000 IU | 2000 IU

2500 IU | 3000 IU | 4000 IU

Important Safety Information
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.

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OCTAPHARMA—A TRUSTED AND RELIABLE SOURCE OF FVIII THERAPY

HOW MUCH DO YOU KNOW ABOUT THE COMPANY THAT MANUFACTURES YOUR HEMOPHILIA A TREATMENT?

Since its founding in 1983, Octapharma has remained true to its principle of enhancing the lives of patients around the world. Today, Octapharma is the largest privately-owned protein products manufacturer in the world.

Octapharma was the first company to apply the solvent/detergent virus inactivation process to the routine production of FVIII concentrates.

Octapharma was also the first company to introduce a rFVIII that's produced in human cells *without chemical modification or fusion with any other protein*. That product is NUWIQ.

In addition to providing world-class coagulation factors, Octapharma provides services and support for the Hemophilia community.

octapharma®

PROGRAMS AND SUPPORT SERVICES

The **NUWIQ Co-Pay Assistance Program** offers eligible patients a savings of up to $12,000 per year on the out-of-pocket costs associated with treatment. To be eligible, you must be receiving treatment with NUWIQ or have a prescription to begin treatment. You must also have commercial health insurance or self-pay. Patients with Medicare, Medicaid, DoD, Tricare, or other federal or state government insurance are not eligible for the program.

Co-pay assistance can only be applied to co-payments, deductibles, self-pay, and coinsurance associated with the cost of NUWIQ. The Co-Pay Assistance Program does not cover costs associated with administration of therapy, such as office visits, infusion costs, or other professional services.

The **NUWIQ Free Trial Program** allows eligible patients to receive treatment with NUWIQ (up to 6 doses, not to exceed 20,000 IUs) at no cost. NUWIQ is shipped directly to eligible patients and is administered under the direction and care of their physician.

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NUWIQ is the Only Recombinant FVIII Produced Using Human Cells

Without Chemical Modification or Protein Fusion

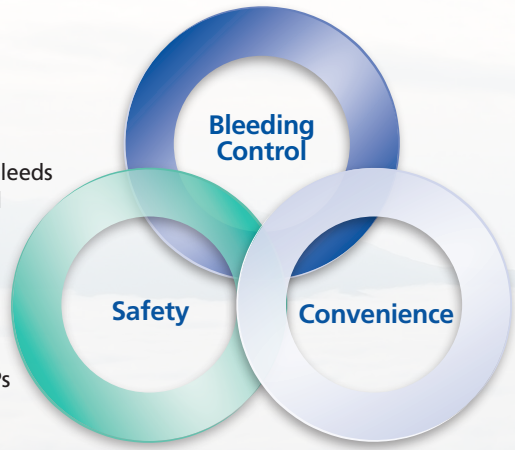
ZERO
Median ABR Spontaneous Bleeds in adults & children

Median ABR for all bleeds was **0.9** in adults and **1.9** in children

LOW INHIBITORS

Zero inhibitors in PTPs

12.8% high-titer inhibitors in PUPs (interim results)



DOSING FLEXIBILITY
2.5 mL diluent volume across ALL vials

Potential for **2X weekly infusions** with personalized prophylaxis

Easy monitoring by chromogenic or one-stage assay

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Octapharma USA, Inc.
117 W. Century Road
Paramus, NJ 07652
Tel: 201-604-1130

Free Trial, Co-Pay Assistance, and Reimbursement
usreimbursement@octapharma.com
Tel: 800-554-4440

Medical Affairs
usmedicalaffairs@octapharma.com

For all inquiries relating to drug safety, or to report adverse events, please contact our local Drug Safety Officer: Tel: 201-604-1137 | Cell: 201-772-4546 | Fax: 201-604-1141 or contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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References: 1. Cafuir LA, Kempton CL. Ther Adv Hematol. 2017;8(10):303–313. **2.** Sandberg H, et al. Thromb Res. 2012;130(5):808-817. **3.** Casademunt E, et al. Eur J Haematol. 2012;89(2):165-176. **4.** Matino D, et al. Haemophilia. 2014;20(2):200-206. **5.** NUWIQ Full Prescribing Information. Hoboken, NJ: Octapharma; rev 2017. **6.** Liesner RJ, et al. Haemophilia. 2018;24(2):211-220. **7.** Lissitchkov T, et al. Haemophilia. 2017;23(5):697-704. **8.** Kannicht C, et al. Thromb Res. 2013;131(1):78-88. **9.** Peyvandi F, Mannucci PM, Garagiola I, et al. N Engl J Med. 2016;374(21):2054-2064.

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