Factor Replacement Therapies
from **Octapharma**

NUWIQ®
Antihemophilic Factor
(Recombinant)

wilate®
von Willebrand
Factor/Coagulation
Factor VIII Complex
(Human)

A Guide for **Patients, Parents, & Caregivers**

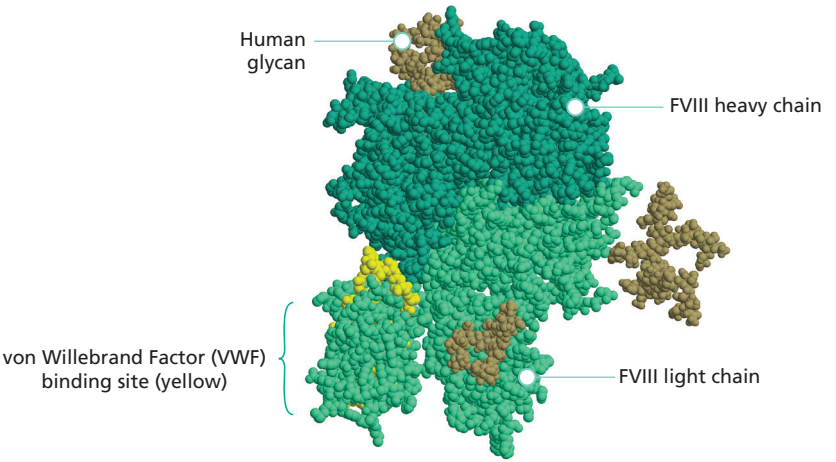
Please see accompanying full Prescribing Information.

octapharma

NUWIQ®—A *Natural Choice* for Your Hemophilia A Treatment

- Factor VIII (FVIII) replacement therapy is the standard of care for hemophilia A[1]
- NUWIQ is a recombinant factor VIII (rFVIII) replacement therapy used to treat hemophilia A in adults and children[2]
- NUWIQ is made using human cells, unlike some other rFVIII products that are made from hamster cells[3,4]

NUWIQ Closely Resembles Natural FVIII Produced in the Human Body[2,3,5,6]



NUWIQ is the only rFVIII produced in human cells without chemical modification or protein fusion.[3,4]
We call it **A *Natural* Choice.**

- NUWIQ was shown to be effective in controlling bleeding in both children and adults[2,7-10]
- NUWIQ had **ZERO** inhibitors in PTPs and a low incidence of inhibitors in a clinical study with PUPs[2,7]
- NUWIQ has the potential to extend your dosing interval with personalized prophylaxis[6]
- NUWIQ is available in a wide range of dosage strengths for individual dosing needs[2]

PTPs = previously treated patients; PUPs = previously untreated patients.

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.

Please see Important Safety Information throughout.

Powerful Bleeding Control in PTPs

Prophylaxis With NUWIQ Reduced Bleeding Frequency[2]

Both adults (N=32) and children (N=59) were treated with NUWIQ prophylaxis (given every other day or 3 times per week) for 6 months or longer.

- For *All Bleeds*, the median ABR was **0.9** in adults and **1.9** in children
- For *Spontaneous Bleeds*, the median annual bleeding rate (ABR) was **ZERO** in both adults and children

ABR = annual bleeding rate.

SPONTANEOUS BLEEDS
Adults & Children

On-Demand Treatment With NUWIQ Provided Effective Bleeding Resolution[8-10]

In adults receiving on-demand treatment (N=986 bleeds)

Responses rated as "excellent" or "good"[2]

Bleeds resolved with **1** infusion

Bleeds resolved with **1** or **2** infusions

Most patients had zero or only 1 bleed with NUWIQ prophylaxis.
With on-demand treatment, 9 out of 10 bleeds resolved with 1 infusion.[2,8]

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.

Please see accompanying full Prescribing Information.

NUWIQ®
Antihemophilic Factor (Recombinant)

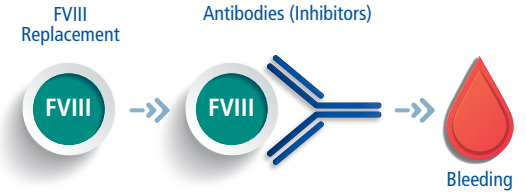
A **Natural** *Choice*

Expressed in a human cell line. B-domain deleted. No chemical modifications.

www.NUWIQUSA.com

Safety With NUWIQ® for Both PTPs and PUPs

Inhibitors Can Impair the Effectiveness of FVIII Treatment[11-13]



- Clinical studies have shown that inhibitors occur in about 30% of people taking FVIII[11,13]
- Risk is higher in PUPs and lowest in PTPs[12]
- High-titer inhibitors are associated with a greater loss of effectiveness of FVIII treatment[13]

The type of FVIII product—made from human cells or hamster cells—together with other factors, can affect inhibitor potential

Inhibitor Incidence and Safety With **NUWIQ**—*Made From Human Cells*[2]

PUPs—Low Rate of Inhibitors With NUWIQ in the *NuProtect* Study (N=105)

- **16.2%** absolute incidence (**17.6%** cumulative incidence) of high-titer inhibitors*

16.2% Absolute Incidence of High-Titer Inhibitors

PTPs—Zero Inhibitors in Patients Who Switched to NUWIQ (N=135)†

- **ZERO** patients experienced serious adverse reactions, anaphylaxis (a very serious allergic reaction), or dropped out of the study because of an adverse reaction to NUWIQ

*Data from 105 PUPs treated with NUWIQ were analyzed for inhibitor development, with 95 patients reaching ≥100 exposure days or inhibitor development.
†In clinical studies with 135 PTPs (74 adults, 3 adolescents, and 58 children), non-neutralizing antibodies without any inhibitor activity were reported in 4 patients (3%).

Inhibitor Incidence With **FVIII Products**—*Made From Hamster Cells or Plasma*[14]

The SIPPET trial (N=251) studied inhibitor rates in PUPs treated with rFVIII products made from hamster cells and FVIII derived from human plasma.

- **28.4%** cumulative incidence of high-titer inhibitors in PUPs treated with hamster-derived FVIII and **18.6%** in PUPs treated with plasma-derived FVIII (pdFVIII)‡

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. The observed incidence of inhibitor formation may be influenced by a number of factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease.

‡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.

Important Safety Information
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.

Please see Important Safety Information throughout.

Dosing Flexibility and Convenience With NUWIQ

NUWIQ Personalized Prophylaxis

Tailor Your Dose and Dosing Frequency—Without Sacrificing Bleeding Control[6]

Personalized prophylaxis for 6 months with NUWIQ enabled the majority of PTPs to extend their dosing frequency to twice weekly or less (*NuPreviq* Study, N=66)[6]

57% 2X OR LESS Weekly Dosing

- Median ABRs for *All Bleeds* was **ZERO**, including spontaneous bleeds, traumatic bleeds, and joint bleeds

NUWIQ Offers a Broad Range of Dosage Strength Vials[2]

Low 2.5 mL diluent volume across the entire range of vial strengths

Watch a step-by-step NUWIQ reconstitution video at *NUWIQUSA.com/Taking NUWIQ*

250 IU | 500 IU | 1000 IU | 2000 IU | 2500 IU | 3000 IU | 4000 IU

- Each NUWIQ box comes with a vial adapter, butterfly needle, and alcohol swabs in addition to the NUWIQ vial and prefilled syringe

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.

Please see accompanying full Prescribing Information.

NUWIQ®
Antihemophilic Factor (Recombinant)

A* Natural *Choice

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www.NUWIQUSA.com

wilate®—Developed Specifically to Treat von Willebrand Disease (VWD)

A Balanced, 1:1 Ratio of von Willebrand Factor (VWF) and FVIII[15]

Unlike other products used to treat VWD, wilate contains equal amounts of VWF and FVIII, similar to the balance that occurs naturally in the body. This may help make dosing and monitoring of treatments easier for you and your doctor.[15-17]

We call this the **Power of Balance**

Low Recommended Dosing For All Types of VWD[15*]

- You may be able to lower the initial dose (also called loading dose) you need to treat bleeds
- You may also be able to increase the amount of time in between your doses for bleeds that require multiple doses (also called maintenance dose)
- Most bleeds are treated for 1 to 3 days, but severe bleeding may need longer treatment

*Based on the Recommended Dosing Guide for wilate. See Dosage and Administration, section 2.1 of full Prescribing Information.

In clinical trials, **93%** of the successfully treated bleeds occurred in type 3 patients, the most severe type of VWD.[15]

*"Since 2005, more than **1 billion** IUs of wilate have been infused worldwide"*[7]

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 also indicated in adolescents and adults with hemophilia A for routine prophylaxis to reduce the frequency of bleeding episodes; and for on-demand treatment and control of bleeding episodes.

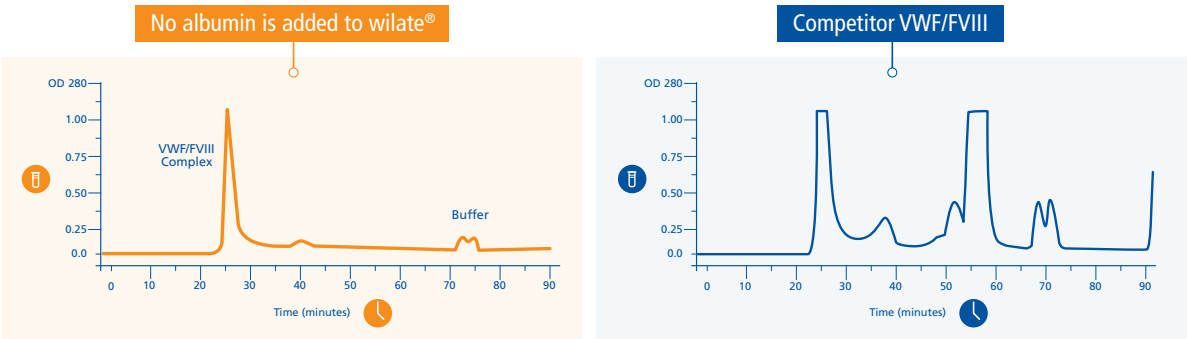
Please see Important Safety Information throughout.

High Purity to Minimize Potential Side Effects

Advanced Purification Process[15]

wilate is purified through a series of steps that minimize impurities and help reduce the risk of side effects. With some other VWF products, proteins (such as albumin) may be added as a stabilizer. With wilate, unwanted proteins are reduced during production—so there is no need to add albumin as a stabilizer.

The figure below shows a single peak with wilate containing only the VWF/FVIII complex.[17]
The competitor product shows additional peaks from other proteins.



High Standards to Ensure Safety

wilate is made from large pools of donated human plasma. All plasma undergoes testing for evidence of a range of viruses, including human immunodeficiency virus, hepatitis B virus, and hepatitis C virus. Any plasma that has evidence of these viruses is rejected.

Double Virus Inactivation | wilate has two dedicated virus inactivation steps to help improve viral safety.[15]

1 **Solvent/Detergent:** Inactivates certain viruses, including HIV, HBV, HCV, and West Nile virus, by breaking down the outer layer.

2 **PermaHeat:** Supplements the S/D process using dry heat (100°C, for 2 hours) to inactivate a broad spectrum of viruses.

HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus.

Important Safety Information
wilate is contraindicated for patients who have known anaphylactic or severe systemic reaction to plasma-derived products, any ingredient in the formulation, or components of the container.

Please see accompanying full Prescribing Information.

wilate®
von Willebrand Factor/Coagulation Factor VIII Complex (Human)

THE POWER OF BALANCE
www.wilateusa.com

Also Approved in Adults and Adolescents With Hemophilia A

Powerful Bleeding Prevention | Prophylaxis[15]

- Prospective, open-label, multicenter clinical study in 55 patients (50 adults, 5 adolescents) treated during 6 months of prophylaxis with 20-40 IU/kg wilate (mean dose, 32 IU/kg)

Median Annualized Bleeding Rate (per subject)

Adults and Adolescents

- **ZERO** All Bleeds
  (range in adults, 0-15.69; range in adolescents, 0-2)
- **ZERO** Spontaneous Bleeds
  (range in adults, 0-11.76; range in adolescents, 0-0)

Effective Bleeding Resolution | On-Demand[15]

96% Managed With 3 or Fewer Injections

- Bleeds were managed with one injection in **63%** of patients, with two injections in **21%**, and with three injections in **12.3%**
- Mean dose per injection, 34 IU/kg

84% of bleeding episodes were treated successfully, with efficacy judged as **GOOD** or **EXCELLENT.**

No PTP treated with wilate developed inhibitors to FVIII

No Serious Systemic Adverse Drug Reactions Were Reported

- Tolerability was assessed in 136 PTPs with hemophilia A (aged 11 to 66 years) treated with wilate in 5 clinical studies. Subjects received over 19 million units of wilate during 9,001 exposure days.
- The most common AE was fever (2 subjects; 1.5%). Other AEs included pruritus (itchy skin), headache and sleeping disorder. The most serious AEs were hypersensitivity reactions, such as allergies and autoimmunity.

AE = adverse event.

Important Safety Information

wilate® is made from human plasma. As with all plasma-derived products, the risk of transmission of infectious agents, eg, viruses and, theoretically, the variant Creutzfeldt-Jakob disease (vCJD) agent or other unknown infectious agents, cannot be completely eliminated. Despite measures to reduce this risk, such products may still potentially transmit disease.

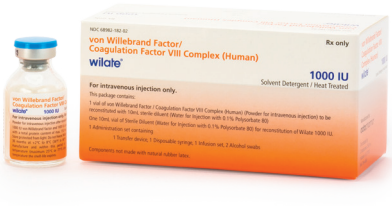
Please see Important Safety Information throughout.

Vial Sizes and Convenience

wilate Is Available in 2 Vial Sizes, 500 or 1000 IU, With a Mix2Vial™ Needle-free Transfer Device[15]

wilate 500 IU

wilate 1000 IU



- wilate is rapidly dissolved in a small injection volume—to help save time during administration
- Includes Mix2Vial™ transfer device—a quick and easy way to mix wilate with less risk of accidental sticks and a built-in filter for a fast and easy process
- Infusion rate with wilate in both VWD and hemophilia A is 2 to 4 mL/minute

Watch a step-by-step wilate reconstitution video at *wilateUSA.com/GettingStarted*

Important Safety Information
Monitor plasma levels of VWF:RCo and FVIII activities in patients receiving wilate to avoid sustained excessive VWF and FVIII activity levels, which may increase the risk of thrombotic events, particularly in patients with known clinical or laboratory risk factors.

Please see accompanying full Prescribing Information.

wilate®
von Willebrand Factor/Coagulation Factor VIII Complex (Human)

THE POWER OF BALANCE

www.wilateusa.com

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Programs and Services

Patient Assistance Made Simple

Free Trial Program

An opportunity for eligible patients with VWD or hemophilia A and their providers to try **NUWIQ** or **wilate**—at no cost—shipped directly to the patient and administered under the care and supervision of the healthcare provider.

NUWIQ®

Eligible patients can receive a free trial of NUWIQ
—not to exceed 6 doses or approximately 20,000 IUs

Call 1-866-830-6541 for more information about the NUWIQ Free Trial

wilate®

Eligible patients can receive a free trial of wilate
—not to exceed 3 doses or approximately 5,000 IUs

Call 1-866-662-1905 for more information about the wilate Free Trial

IU = International Units.

3 Steps to Enroll

1. Download, complete, and sign the **NUWIQ** or **wilate** Free Trial Enrollment and HIPAA forms with your healthcare provider
2. Your healthcare provider will write and hand you a prescription for **NUWIQ** or **wilate**
3. You fax the completed forms and prescription to Program Administrator (Covance) at 1-800-554-6744

For more information, and to download the Free Trials and HIPAA forms, go to the **Patient Support** sections at **nuwiqusa.com** or **wilateusa.com.**

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Co-Pay Assistance Program

Provides Eligible Patients With Significant Savings on Some of the Costs Associated With Treatment

If you are currently using **NUWIQ** or **wilate**, or if you are about to begin therapy, the Octapharma Co-Pay Program can offer savings up to:

$12,000 PER YEAR ON THE OUT-OF-POCKET COSTS ASSOCIATED WITH THERAPY

Program Eligibility and Coverage

You must currently be using a factor product from Octapharma (NUWIQ or wilate), or have a prescription to begin therapy

- You must have commercial insurance
  - — Those with Medicare, Medicaid, Medigap, VA, DOD, Tricare, or other federal or state government insurance are not eligible
- Co-Pay assistance may only be applied to co-payments, deductibles and co-insurance that may be associated with the cost of Octapharma factor products
  - — The Co-Pay Assistance Program does not cover costs associated with administration of therapy, such as office visits, infusion costs, or other professional service

Reimbursement

Octapharma can help with reimbursement for your **NUWIQ** or **wilate** prescriptions.

Contact the **Octapharma Support Center** for help with your reimbursement matters. Octapharma representatives are available to provide expert advice and information about insurance matters including:

- Individual claims processing reviews
- Assistance in appeals
- Insurance investigations into product coverage
- Gaining approvals for prior authorizations for **NUWIQ** or **wilate**

To determine your eligibility for the **Octapharma Co-Pay Program,** or for help with your reimbursement matters, call to speak with an **Octapharma representative.**

NUWIQ
1-800-554-4440

wilate
1-800-554-4440

You can also email us at
usreimbursement@octapharma.com

Please see accompanying full Prescribing Information.

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Contact octapharma

Octapharma USA, Inc. **Corporate Office**	117 W. Century Road, Paramus, NJ 07652 **Tel:** 201-604-1130 | **www.octapharmausa.com**
Customer Service	General questions and product support. **Tel:** 866-766-4860 | **uscustomerservice@octapharma.com**
Octapharma **Medical Affairs**	**usmedicalaffairs@octapharma.com**
To contact your **local Octapharma Representative**	**Tel:** 201-604-1130

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**

octapharmausa.com

Important Safety Information for NUWIQ®

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 with NUWIQ. Early signs of hypersensitivity reactions that can progress to anaphylaxis may include angioedema, chest tightness, dyspnea, wheezing, urticaria, or pruritus. Immediately discontinue administration and initiate appropriate treatment if hypersensitivity occurs.

Important Safety Information for wilate®

Contraindications

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.

Warnings and Precautions

Anaphylaxis and severe hypersensitivity reactions are possible. Thromboembolic events may occur. Monitor plasma levels of FVIII activity. The most common adverse reactions (≥1%) in patients with VWD were hypersensitivity reactions, urticaria, and dizziness. The most serious adverse reactions in patients with VWD were hypersensitivity reactions.

References: 1. Aledort L, et al. Blood Transfus. 2019;17:479-486. **2.** NUWIQ full Prescribing Information. Paramus NJ: Octapharma; rev 2020. **3.** Sandberg H, et al. Thromb Res. 2012;130:808-817. **4.** Casademunt E, et al. Eur J Haematol. 2012;89(2):165-176. **5.** Cafuir LA, et al. Ther Adv Hematol. 2017;8(10):303–313. **6.** Lissitchkov T, et al. Haemophilia. 2017;23:697-704. **7.** Data on file, Octapharma, Inc. **8.** Valentino LA, et al. Haemophilia. 2014;20(suppl 1):1-9. **9.** Kessler C, et al. Haemophilia. 2015;21(suppl 1):1–12. **10.** Lissitchkov T, et al. Haemophilia. 2016;22:225-231. **11.** Witmer C, Young G. Ther Adv Hematol. 2013;4(1):59-72. **12.** van den Berg, HM. Thromb J. 2016;14(suppl 1):31. **13.** Hemophilia Federation of America. Inhibitors. Available at: https://www.hemophiliafed.org/understanding-bleeding-disorders/complications/inhibitors **14.** Peyvandi F, et al. N Engl J Med. 2016;374:2054-2064. **15.** wilate® full Prescribing Information. Paramus NJ: Octapharma; rev 2019. **16.** Kessler CM, et al. Thromb Haemost. 2011;106:279-288. **17.** Stadler M, et al. Biologicals. 2006;34:281-288.

Please see Important Safety Information throughout.
Please see accompanying full Prescribing Information.

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