



ADYNOVATE
[Antihemophilic Factor
(Recombinant), PEGylated]

NEW

**ADYNOVATE IN PREVIOUSLY
UNTREATED PATIENTS (PUPS)
WITH SEVERE HEMOPHILIA A**

**Results from a Phase 3, Prospective, Multicenter,
Open-Label Clinical Trial in PUPs¹**

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

Indications and Limitation of Use

ADYNOVATE is indicated in adult and pediatric patients with hemophilia A (congenital factor VIII deficiency) for:

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

ADYNOVATE is not indicated for the treatment of von Willebrand disease.

SELECTED IMPORTANT RISK INFORMATION

CONTRAINDICATIONS

ADYNOVATE is contraindicated in patients who have had prior anaphylactic reaction to ADYNOVATE, to the parent molecule (ADVATE [Antihemophilic Factor (Recombinant)]), mouse or hamster protein, or excipients of ADYNOVATE (e.g. Tris, mannitol, trehalose, glutathione, and/or polysorbate 80).

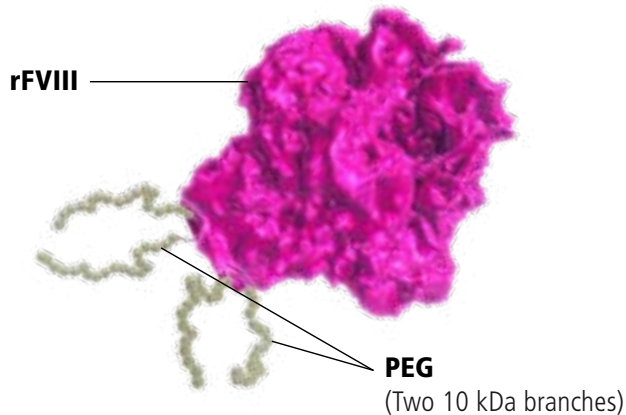
Please see ADYNOVATE Important Risk Information throughout this brochure.
Click [here](#) for ADYNOVATE Full Prescribing Information.



AN ESTABLISHED EXTENDED HALF-LIFE FVIII THERAPY WITH PROVEN EXPERIENCE²

ADYNOVATE
[Antihemophilic Factor
(Recombinant), PEGylated]

Initially approved in 2015, ADYNOVATE is indicated for on-demand treatment and control of bleeding episodes, perioperative management, and routine prophylaxis in adults and children with hemophilia A.²



- ADYNOVATE is a full-length rFVIII protein, built on the proven molecule of ADVATE, and designed to extend FVIII circulation time with its two 10 kDa arms of PEG²
- The extended terminal half-life of ADYNOVATE was 1.3X-1.5X longer than that of ADVATE in children under 12 years old and 1.4X-1.5X longer in adolescents and adults 12 years and older²⁻⁴
- PEGylation technology* was deliberately chosen to allow for half-life extension while maintaining the integrity of the ADVATE protein. It has a long history of use as an extension technology^{5,6}

- 5.5 billion IUs of ADYNOVATE sold globally^{7†}

EFFICACY AND SAFETY PROFILE ESTABLISHED IN CLINICAL TRIALS OF PEDIATRIC AND ADULT PATIENTS AND SUPPORTED BY REAL-WORLD EXPERIENCE FOR OVER 11 YEARS.²

*PEGylation is the covalent attachment of a PEG to a drug or protein. Proprietary PEGylation Technology exclusively licensed from Nektar Therapeutics.⁵

[†]As of November 2024.⁷

FVIII=factor VIII; IU=international unit; PEG=polyethylene glycol; rFVIII=recombinant factor VIII.

SELECTED IMPORTANT RISK INFORMATION

WARNINGS & PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have been reported with ADYNOVATE. Hypersensitivity reactions that can progress to anaphylaxis may include angioedema, chest tightness, dyspnea, wheezing, urticaria, pruritus, and nausea and vomiting. Immediately discontinue administration and initiate appropriate treatment if hypersensitivity reactions occur.

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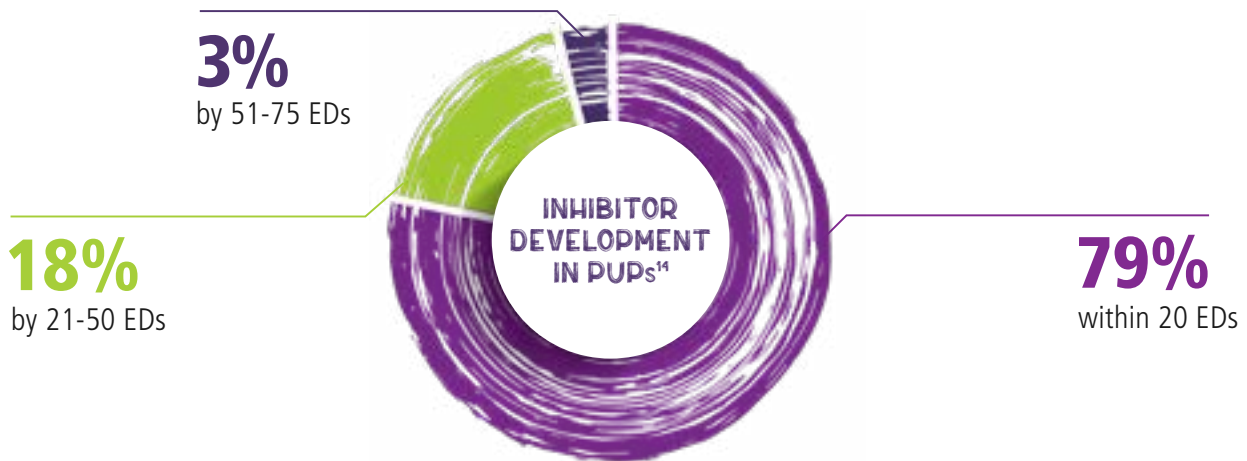
INHIBITOR DEVELOPMENT IN PUPS

FVIII inhibitors typically develop following FVIII-replacement treatment, including plasma-derived products, in ~30% of PUPs⁸⁻¹⁶

- The development of FVIII inhibitors results in serious treatment complications such as more frequent bleeding (including life-threatening bleeds), which can cause the management of bleeds to become challenging¹⁷
- Genetics, family history, and environmental factors play a role in inhibitor development, with several mutations identified as being associated with increased inhibitor risk¹⁷

A prospective global registry* tracking newly diagnosed hemophilia A patients (N=1038) found¹⁴:

97% of inhibitors develop within 50 days, with 79% occurring in the first 20 days of treatment¹⁴



➤ Results of a phase 3 trial of inhibitor development rates in PUPs treated with ADYNOVATE are presented further in this brochure.^{1,2}

*Aiming to define the risk periods for inhibitor development until 1000 EDs.¹⁴
ED=exposure day; PUP=previously untreated patient.

SELECTED IMPORTANT RISK INFORMATION

WARNINGS & PRECAUTIONS

Neutralizing Antibodies

Formation of neutralizing antibodies (inhibitors) to factor VIII can occur following administration of ADYNOVATE. Monitor patients regularly for the development of factor VIII inhibitors by appropriate clinical observations and laboratory tests. Perform an assay that measures factor VIII inhibitor concentration if the plasma factor VIII level fails to increase as expected, or if bleeding is not controlled with expected dose.

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SAFETY AND EFFICACY WERE EVALUATED IN 120 PUPS^{1,2}

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STUDY DESCRIPTION

- A prospective, multicenter, Phase 3, open-label trial evaluated ADYNOVATE in 120 previously untreated pediatric patients (<6 years, severe hemophilia A, FVIII <1%)^{1,2}
- Eligible patients had ≤ 2 prior FVIII exposure days and no inhibitors at enrollment¹
- Participants received either prophylaxis or on-demand therapy¹
- Immunogenicity was evaluated by monitoring neutralizing (inhibitory) antibodies to FVIII and by measuring the development of binding IgG and IgM antibodies against factor VIII, PEGylated (PEG)-factor VIII, and PEG using validated ELISA assays^{1,7}
- Treatment continued for ≥ 100 exposure days or until inhibitor development¹
- The study spanned 55 sites in 19 countries, with data collected on demographics and eligibility: White (50.8%), Asian (37.5%), Black or African American (5.8%), Hispanic or Latino (5%), Multiple Races (3.3%), Other Races (2.5%)⁷
- The study began in November 2015, with the final database lock in December 2024⁷

STUDY OBJECTIVE

To investigate the safety, immunogenicity, and hemostatic efficacy of ADYNOVATE with the incidence of FVIII inhibitor development as primary outcome.¹

ELISA=enzyme-linked immunosorbent assay.

SELECTED IMPORTANT RISK INFORMATION

ADVERSE REACTIONS

The most common adverse reactions ($\geq 1\%$ of patients) reported in the clinical studies were cough, headache, diarrhea, vomiting, rash, nausea, urticaria, and dizziness.

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11% OF PUPS DEVELOPED FVIII INHIBITORS^{2,7}

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From the completed study in 120 PUPs with severe hemophilia A^{2,7}



*The remaining 20 patients had <100 EDs when they discontinued or completed the analysis and therefore were not included in the evaluation.⁷
SD=standard deviation.

Of the 11 patients who developed FVIII inhibitors, 6 developed high titer inhibitors (>5 Bethesda Units) and 5 developed low titer inhibitors (≤5 Bethesda Units).²

A LOW INHIBITOR DEVELOPMENT RATE OF 11% WAS OBSERVED IN THE ADYNOVATE PUP STUDY²

Formation of neutralizing antibodies (inhibitors) to FVIII can occur following administration of ADYNOVATE. Monitor patients regularly for the development of FVIII inhibitors by appropriate clinical observations and laboratory tests.²

➤ **Discuss the low inhibitor development rate of ADYNOVATE found in the PUP study with your patients and/or their caregivers for on-demand needs.**

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NOAH, 3

- Houston, TX
- Pre-Kindergarten
- Severe hemophilia A on non-factor prophylaxis

Hypothetical patient

TREATMENT CONSIDERATIONS FROM NOAH'S HCP:

- ADYNOVATE is a full-length recombinant FVIII protein with an extended terminal half-life, lasting longer in the body than standard half-life FVIII products^{2,3}
- ADYNOVATE efficacy and safety profile has been proven in clinical studies and supported by real-world experience for the past 10 years²
- In a study with patients who hadn't received FVIII treatment before, ADYNOVATE:
 - Had a low rate of inhibitor development (11%)²

Formation of neutralizing antibodies (inhibitors) to FVIII can occur following administration of ADYNOVATE. Monitor patients regularly for the development of FVIII inhibitors by appropriate clinical observations and laboratory tests.²

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Hypersensitivity Reactions

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MY CHILD'S HEMOPHILIA A STORY

- Shortly after birth, our doctor prescribed my son a non-factor prophylaxis therapy
- Recently, he fell at the playground and injured his knee, resulting in a bleed that required FVIII infusion. Our HCP administered ADYNOVATE to control the bleed
- We discussed FVIII options with our HCP, who highlighted the potential risk of developing an inhibitor, which could complicate treatment
- Following this incident, we decided to continue using ADYNOVATE for on-demand and surgery needs, including any emergency visits and future surgeries, such as the possible tonsillectomy and tooth extraction mentioned by his HCP

WHY DID NOAH'S HCP CHOOSE ADYNOVATE?

Do you have patients like Noah, who could benefit from ADYNOVATE on-demand?

➤ **When it comes to a low inhibitor development rate (11% in a clinical study) and bleed control, choose ADYNOVATE for your PUPs' on-demand needs²**

Individual results may vary.

ADYNOVATE IN PREVIOUSLY UNTREATED PATIENTS (PUPS)

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INHIBITOR DEVELOPMENT CAN OCCUR IN PUPS WITH FVIII REPLACEMENT TREATMENT, INCLUDING PLASMA-DERIVED PRODUCTS⁸

- FVIII inhibitors can lead to serious complications such as increased bleeding (including life-threatening bleeds), making bleed management more difficult¹

ADYNOVATE, AN EXTENDED HALF-LIFE FVIII THERAPY WITH PROVEN EXPERIENCE

- Established efficacy and safety profile supported by real-world experience for over 10 years²
- 5.5 billion IUs of ADYNOVATE sold globally^{7*}

ADYNOVATE WAS STUDIED IN 120 PUPS

- Pediatric patients <6 years old with severe Hemophilia A (FVIII <1%)^{1,2}
- Study conducted from November 2015 to December 2024⁷

ADYNOVATE DEMONSTRATED A LOW INHIBITOR DEVELOPMENT RATE IN PUPS²

- Of the 100 PUP patients evaluable for inhibitor development, 11 patients developed FVIII inhibitors while 89 did not^{2†}

WHEN IT COMES TO A LOW INHIBITOR DEVELOPMENT RATE (11% IN A CLINICAL STUDY) AND BLEED CONTROL, CHOOSE ADYNOVATE FOR YOUR PUPS' ON-DEMAND NEEDS²

Formation of neutralizing antibodies (inhibitors) to FVIII can occur following administration of ADYNOVATE. Monitor patients regularly for the development of FVIII inhibitors by appropriate clinical observations and laboratory tests.²

*As of November 2024.⁷

†100 PUPs were evaluable for inhibitor development, 11 patients developed FVIII inhibitors while 89 did not.^{1,2,7}

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