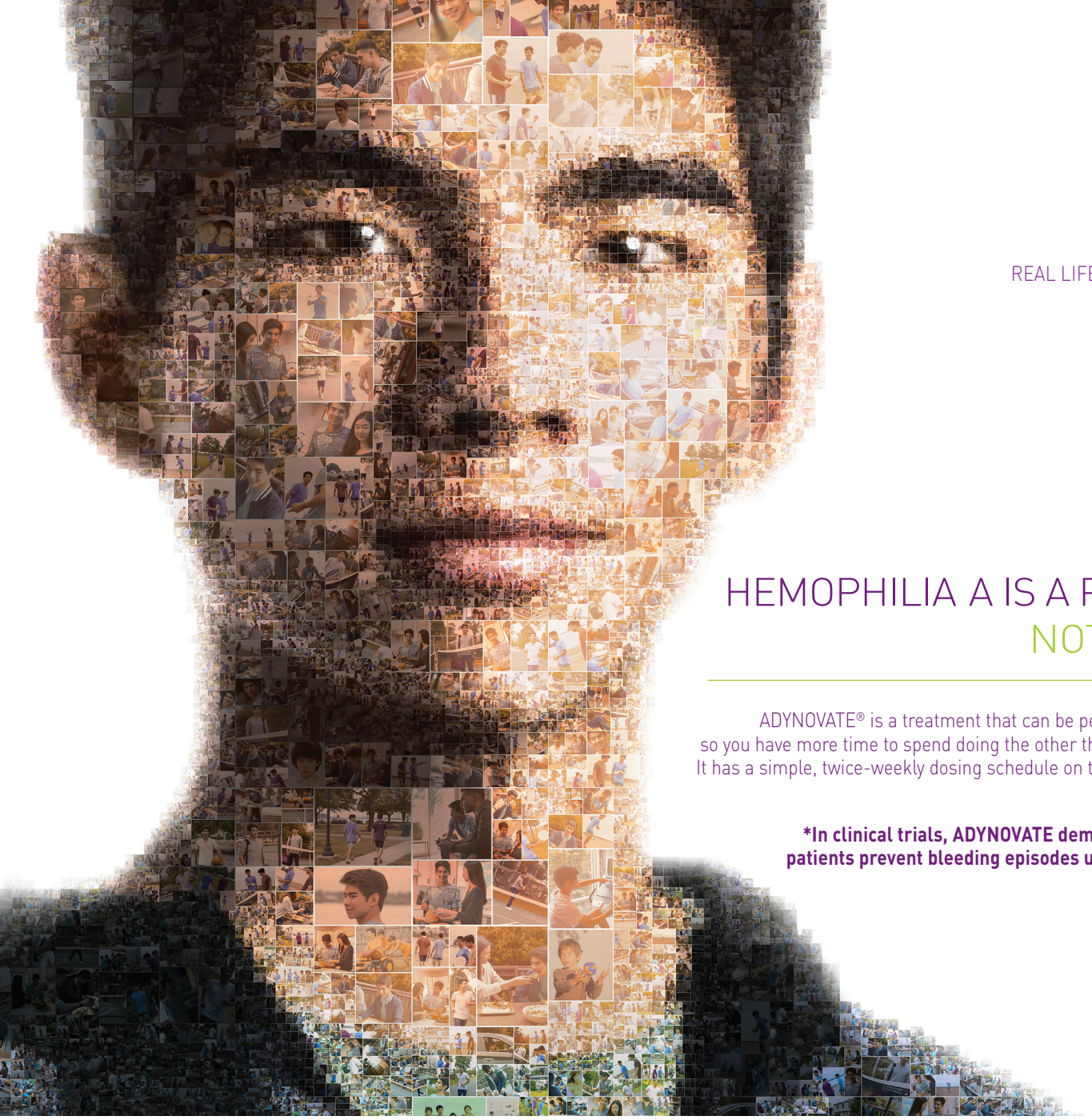


ADYNOVATE
[Antihemophilic Factor (Recombinant), PEGylated]

REAL LIFE. REAL BLEED PROTECTION.*

HEMOPHILIA A IS A PIECE OF YOU. NOT ALL OF YOU.

ADYNOVATE® is a treatment that can be personalized to fit your lifestyle so you have more time to spend doing the other things that also make you, you. It has a simple, twice-weekly dosing schedule on the same 2 days every week.[1,2]

***In clinical trials, ADYNOVATE demonstrated the ability to help patients prevent bleeding episodes using a prophylaxis regimen.**

No actual patients depicted.

ADYNOVATE Important Information

What is ADYNOVATE?

- ADYNOVATE is an injectable medicine that is used to help treat and control bleeding in children and adults with hemophilia A (congenital Factor VIII deficiency).
- Your healthcare provider (HCP) may give you ADYNOVATE when you have surgery.
- ADYNOVATE can reduce the number of bleeding episodes when used regularly (prophylaxis).

ADYNOVATE is not used to treat von Willebrand disease.

SELECTED IMPORTANT RISK INFORMATION

Who should not use ADYNOVATE?

Do 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 HCP if you are pregnant or breastfeeding because ADYNOVATE may not be right for you.

Please see ADYNOVATE Important Risk Information throughout this brochure and Detailed Important Risk Information on back cover.
For additional safety information, please click HERE for ADYNOVATE Full Prescribing Information and discuss with your HCP.

Clicking this link leads to: http://www.shirecontent.com/PI/PDFs/ADYNOVATE_USA_ENG.pdf

ADYNOVATE
[Antihemophilic Factor (Recombinant), PEGylated]

REAL LIFE. REAL BLEED PROTECTION.*

PROVEN PROPHYLAXIS

ADYNOVATE provides proven bleed protection*

95%
reduction in median ABR

When changing from on-demand use to prophylaxis

41.5 (IQR:19.4) median ABR with on-demand treatment versus 1.9 (IQR:5.9) median ABR with prophylactic treatment.[1,3]

ABR=Annualized bleed rate; IQR=Interquartile range.
Median is defined as the middle number in a list of numbers arranged in numerical order.

Clinical study design

A clinical trial of 137 previously treated patients (age 12 years and older) with severe hemophilia A evaluated how well ADYNOVATE worked over 6 months, in both twice-weekly prophylaxis and on-demand use. 120 patients received a prophylaxis dose of 40-50 IU/kg twice a week, and 17 received an on-demand dose of 10-60 IU/kg. The main objective of the study was to compare the annualized bleed rates in the patients receiving prophylaxis and those receiving on-demand treatment.[1]

ADYNOVATE is approved for both on-demand and prophylaxis use in patients with hemophilia A to help with bleeding episodes.[1]

***In clinical trials, ADYNOVATE demonstrated the ability to help patients prevent bleeding episodes using a prophylaxis regimen.**

SELECTED IMPORTANT RISK INFORMATION

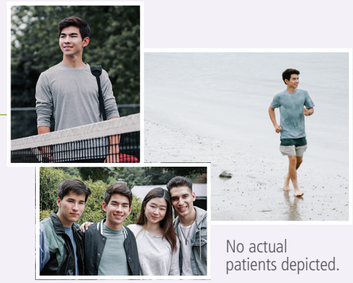
What should I tell my HCP before using ADYNOVATE?

Tell your HCP 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 or 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 important information do I need to know about 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.
- Do not attempt to infuse yourself with ADYNOVATE unless you have been taught by your HCP or hemophilia center.



No actual patients depicted.

Effective coverage against bleeds

zero
Median ABR
for joint & spontaneous bleeds in 120 patients[1]

Joint bleeds:

38.1 (IQR:20.1) median ABR with on-demand versus 0.0 (IQR:2.0) median ABR with prophylaxis[1,3]

Spontaneous bleeds:

21.6 (IQR:22.0) median ABR with on-demand versus 0.0 (IQR:2.2) median ABR with prophylaxis[1,3]

Prophylaxis also helped many stay bleed-free

40% (40 out of 101 patients)†
experienced zero total bleeds[1]

†Results from patients who met the requirements to complete the study.

- 57% of 120 patients experienced zero joint bleeds[1]
- 57% of 120 patients experienced zero spontaneous bleeds[3]

SELECTED IMPORTANT RISK INFORMATION

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. Talk with your HCP to make sure you are carefully monitored with blood tests for the development of inhibitors to factor VIII.

What are possible side effects of ADYNOVATE?

- The common side effects of ADYNOVATE are headache and nausea. These are not all the possible side effects with ADYNOVATE. Tell your HCP about any side effects that bother you or do not go away.

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ADYNOVATE
[Antihemophilic Factor (Recombinant), PEGylated]

REAL LIFE. REAL BLEED PROTECTION.*

ESTABLISHED SAFETY PROFILE

zero

inhibitors to ADYNOVATE

were reported in 237 previously treated patients in clinical studies[1]

- In 191 adults and children previously treated for at least 50 days with ADYNOVATE, zero factor VIII inhibitors developed[1†]
- 1 previously untreated patient who received at least 1 infusion of ADYNOVATE did develop neutralizing antibodies to factor VIII[1]

Pooled safety data evaluation[1]

The safety of ADYNOVATE was measured in children and adults with severe hemophilia A who received at least 1 dose of ADYNOVATE in 3 completed clinical studies and 4 ongoing clinical studies.

Further immune system response evaluation[1]

The development of antibodies against factor VIII, PEGylated (PEG)-factor VIII, and PEG and Chinese hamster ovary (CHO) protein also were measured in these trials.

- Most patients (238/243) with at least 1 infusion of ADYNOVATE did not develop a persistent antibody response
- At 1 or 2 consecutive study visits, 13 patients who tested negative at screening developed antibodies against factor VIII (6 out of 13) or PEG-FVIII (8 out of 13)
- The antibodies developed were only there for a short time and were not found at subsequent study visits

***In clinical trials, ADYNOVATE demonstrated the ability to help patients prevent bleeding episodes using a prophylaxis regimen.**

†Children: <6 years of age with ≥50 days of treatment with ADYNOVATE, age ≥6 to <12 years of age with ≥150 days of treatment with ADYNOVATE. Adolescent and adult patients are ≥12 years old with ≥150 prior days of treatment with ADYNOVATE.

SELECTED IMPORTANT RISK INFORMATION

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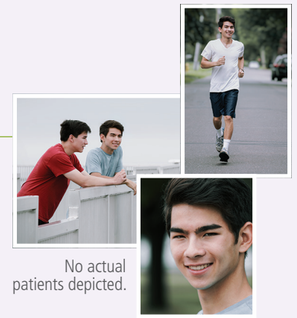
DOSING SCHEDULE CAN BE PERSONALIZED FOR A CHANGING LIFESTYLE



No actual patients depicted.

ADYNOVATE has been designed to stay in your body longer, so you can have more time to spend being you between infusions. Twice-weekly infusions with a simple dosing schedule, taken on the same 2 days every week, allows your treatment schedule to work with your real-life needs—the same 2 days you infuse each week are up to you.[1,4]

Clinical study design

A clinical study of 26 patients with severe hemophilia A (at least 12 years old) compared doses of ADYNOVATE with doses of ADVATE® [Antihemophilic Factor (Recombinant)]. Results found that ADYNOVATE stays in the body of patients 12 years and older 1.4 to 1.5 times longer than ADVATE.[4]

Twice Weekly[1]

70%

of patients age 12 or older

(69 out of 98 in a clinical study) were able to reduce the frequency of their prophylaxis dosing by approximately 1 fewer infusion per week from their pre-study prophylaxis routine.[3]

What would you do if you didn't have to infuse as often each week as you do now? How would your schedule change?

Everyone's body and daily routine is different, so talk with your doctor to see if ADYNOVATE can work within your schedule.[2]

SELECTED IMPORTANT RISK INFORMATION

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SUPPORT THROUGHOUT THE TREATMENT JOURNEY

FREEDOM OF CHOICE™ Program

FREE-TRIAL PROGRAM

You may be eligible to receive 8 free-trial doses of ADYNOVATE with the FREEDOM OF CHOICE trial program. The free trial program is for new patients only. Participants must receive consultation and approval from their healthcare provider. For more information, visit **www.adynovate.com**.

Clicking this link leads to: www.adynovate.com

Takeda's CoPay Assistance Program

For eligible patients, learn how our CoPay Assistance Program may cover out-of-pocket expenses related to treatment that requires a co-pay, up to the program maximum.

Hematology Support Center

Hematology Support Center (HSC) is a dedicated team that helps patients who have been prescribed Takeda Hematology products with information, guidance, and resources regarding treatment.

Learn more by calling **1-888-229-8379** Monday–Friday 8:30AM–8:00PM ET or online at **www.hematologysupport.com**.

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ADYNOVATE is covered* on [over 90%†] of commercial and Medicaid health plans[5]

Please talk to your doctor for more information about ADYNOVATE.

*Source: FINGERTIP FORMULARY®, as of [04/06/2020], is subject to change without notice by a health plan or state.
†Product coverage divided by total therapeutic category coverage, based on the Rx and Medical coverage using DRG medical lives.

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DETAILED IMPORTANT RISK INFORMATION

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REFERENCES: 1. ADYNOVATE Prescribing Information. **2.** Valentino LA. Considerations in individualizing prophylaxis in patients with haemophilia A. *Haemophilia*. 2014;20(5):607-615. **3.** Takeda data on file. **4.** Konkle BA, Stasyshyn O, Chowdary P, et al. Pegylated, full-length, recombinant factor VIII for prophylactic and on-demand treatment of severe hemophilia A. *Blood*. 2015;126(9): 1078-1085. **5.** Decision Resources Group: Fingertip Formulary Analytics 2.0, Accessed March 1, 2019.