ADVATE Important Information

What is ADVATE?

- ADVATE 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).
- ADVATE is used to prevent and control bleeding in adults and children (0-16 years) with hemophilia A. Your healthcare provider (HCP) may give you ADVATE when you have surgery.
- ADVATE can reduce the number of bleeding episodes in adults and children (0-16 years) when used regularly (prophylaxis).

ADVATE is not used to treat von Willebrand disease.

Please see ADVATE Important Risk Information located throughout this brochure and Important Facts about ADVATE at the end of the brochure.

SELECTED IMPORTANT RISK INFORMATION

Who should not use ADVATE?

Do not use ADVATE if you:
- Are allergic to mice or hamsters.
- Are allergic to any ingredients in ADVATE.

Tell your HCP if you are pregnant or breastfeeding because ADVATE may not be right for you.

ADVATE has over 15 years of treatment experience in the real world and provides clinically proven bleed protection* for people with hemophilia A.

*In clinical trials, ADVATE demonstrated the ability to help prevent bleeding episodes using a prophylaxis regimen.
In an open-label, randomized, controlled clinical study of the efficacy of ADVATE use in 2 prophylactic treatment regimens compared to that of on-demand treatment, 53 previously treated patients (PTPs) with severe to moderately severe hemophilia A were analyzed in the per-protocol group. Patients were initially treated for 6 months of on-demand therapy and then randomized to 12 months of either a standard prophylaxis regimen (20–40 IU/kg every 48 hours) or a pharmacokinetic-driven prophylaxis regimen (20–80 IU/kg every 72 hours). ABRs for the two prophylaxis regimens were comparable.

In a clinical trial, 0 bleeds in 42% of patients during 1 year on the prophylaxis (n=22 in the per-protocol group of 53). Per-protocol: subjects who had >90% of the predicted number of infusions and no major protocol deviations.

In a clinical trial, 98% reduction in median ABR from 44 to 1 when patients switched from on-demand to prophylaxis.

SELECTED IMPORTANT RISK INFORMATION (continued)
What should I tell my HCP before using ADVATE?
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 ADVATE passes into your milk and it can harm your baby.

Are or become pregnant. It is not known if ADVATE may harm your unborn baby.

Have been told that you have inhibitors to factor VIII (because ADVATE may not work for you).
Established safety profile1,3,4

The safety of ADVATE was evaluated in 8 studies in 276 PTPs with moderately severe to severe hemophilia A. PTPs were defined as having ≥50 or ≥150 exposure days (EDs) to FVIII products, depending on the study. In this analysis, PTPs were defined as patients with ≥50 EDs. For PTP inhibitor incidence, all PTPs with ≥10 consecutive EDs (N=276) during the course of individual studies were included in the analysis. EDs were defined as calendar days on which rAHF-PFM was administered.3

What important information do I need to know about ADVATE?

- You can have an allergic reaction to ADVATE. Call your HCP 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 ADVATE unless you have been taught by your HCP or hemophilia center.

In clinical trials, ADVATE demonstrated the ability to help patients prevent bleeding episodes using a prophylaxis regimen.
Access Personalization and Support

With the myPKFiT® for ADVATE® Patients Mobile App

In the US, myPKFiT is intended to be used with ADVATE patients who are 16 years of age or older with a body weight of 45 kg or greater.

Proven clinical experience

15+ Years of Real-World Experience
Third-generation full-length molecule, similar to the factor VIII that occurs naturally in the body.

Extensively Studied
Evidence spanning over 15 years from 15 prospective studies.

The Most Widely Used FVIII Product†
With 33 billion International Units (IUs) sold worldwide.

†Based on units sold, as of July 2018.

myPKFiT® for ADVATE Patients Mobile Application

Intended Use

• The myPKFiT for Patients Mobile Application ("myPKFiT Mobile App") is intended for use by patients with hemophilia A being treated with ADVATE [Antihemophilic Factor (Recombinant)] who are 16 years of age or older with a body weight of 45 kg or greater, and their caregivers.
• The myPKFiT Mobile App is designed to make it convenient for you to record your infusion and bleed events, track your estimated Factor VIII levels following a prophylactic infusion, and export the data for review by your healthcare provider ("HCP").
• Your HCP can use the myPKFiT software to generate ADVATE dosage amount and frequency recommendations for routine prophylaxis using your age, body weight information, and laboratory tests that measure your Factor VIII clotting activity. Using myPKFiT software, HCPs can evaluate various prophylaxis dose regimens tailored to your individual needs and treatment plan.
• myPKFiT Mobile App should only be used by hemophilia A patients treated with ADVATE, as per the ADVATE Prescribing Information.
• myPKFiT Mobile App is not indicated for use by patients with von Willebrand disease. myPKFiT Mobile App should not be used by patients who have developed inhibitors to Factor VIII products.

myPKFiT for Patients Mobile Application is Rx only. For safe and proper use of the myPKFiT Mobile App, please refer to the complete instructions for use in the User Manual.
FREE-TRIAL PROGRAM

ADVATE with BAXJECT III® Instructions

Learn how to reconstitute your medication, including easy one-step activation for reconstituting the ADVATE in a BAXJECT III system. Visit the ADVATE channel on www.YouTube.com to access the instructional videos. You should be trained on how to do infusions by your healthcare provider or hemophilia treatment center.

What are possible side effects of ADVATE?
• Side effects that have been reported with ADVATE include: cough, headache, joint swelling/aching, sore throat, fever, itching, unusual taste, dizziness, hematoma, abdominal pain, hot flashes, swelling of legs, diarrhea, chills, runny nose/congestion, nausea/vomiting, sweating, and rash. Tell your HCP about any side effects that bother you or do not go away or if your bleeding does not stop after taking ADVATE.

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 their treatment. Learn more at 888-229-8379 Monday–Friday 8:30AM–8:00PM ET or online at www.hematologysupport.com.

SELECTED IMPORTANT RISK INFORMATION (continued)

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• Side effects that have been reported with ADVATE include: cough, headache, joint swelling/aching, sore throat, fever, itching, unusual taste, dizziness, hematoma, abdominal pain, hot flashes, swelling of legs, diarrhea, chills, runny nose/congestion, nausea/vomiting, sweating, and rash. Tell your HCP about any side effects that bother you or do not go away or if your bleeding does not stop after taking ADVATE.

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.

For additional safety information, please see Important Facts about ADVATE on the following page and discuss with your HCP.

For full Prescribing Information, visit www.ADVATE.com.

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

Support throughout the treatment journey

FREEDOM OF CHOICE™ Program

You may be eligible to receive 6 free-trial doses of ADVATE 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.advate.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.

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SELECTED IMPORTANT RISK INFORMATION (continued)

What are possible side effects of ADVATE?
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For additional safety information, please see Important Facts about ADVATE on the following page and discuss with your HCP. For full Prescribing Information, visit www.ADVATE.com.

Please see ADVATE Important Risk Information located throughout this brochure and Important Facts about ADVATE at the end of the brochure.
Important facts about ADVATE

**ADVATE [Antihemophilic Factor (Recombinant)]**

This leaflet summarizes important information about ADVATE. 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 ADVATE. If you have any questions after reading this, ask your healthcare provider.

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

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 ADVATE so that your treatment will work best for you.

**What is ADVATE?**

ADVATE 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). The product does not contain plasma or albumin. Hemophilia A is an inherited bleeding disorder that prevents blood from clotting normally. ADVATE is used to prevent and control bleeding in adults and children (0-16 years) with hemophilia A.

Your healthcare provider may give you ADVATE when you have surgery. ADVATE can reduce the number of bleeding episodes in adults and children (0-16 years) when used regularly (prophylaxis). ADVATE is not used to treat von Willebrand disease.

**Who should not use ADVATE?**

You should not use ADVATE if you:
- Are allergic to mice or hamsters.
- Are allergic to any ingredients in ADVATE.

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

**How should I use ADVATE?**

ADVATE is given directly into the bloodstream.

You may infuse ADVATE 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 ADVATE by themselves or with the help of a family member.

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

You may have to have blood tests done after getting ADVATE 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 ADVATE.

**What should I tell my healthcare provider before I use ADVATE?**

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-thecounter medicines, supplements or herbal remedies.
- Have any allergies, including allergies to mice or hamsters.
- Are breastfeeding. It is not known if ADVATE passes into your milk and if it can harm your baby.
- Are pregnant or planning to become pregnant. It is not known if ADVATE may harm your unborn baby.
- Have been told that you have inhibitors to factor VIII (because ADVATE may not work for you).

**What are the possible side effects of ADVATE?**

You can have an allergic reaction to ADVATE.

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.

Side effects that have been reported with ADVATE include:

- Cough
- Sore throat
- Unusual taste
- Abdominal pain
- Diarrhea
- Nausea/vomiting
- Headache
- Fever
- Dizziness
- Hot flashes
- Chills
- Swelling
- Sweating
- Runny nose/congestion
- Rash

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 ADVATE. You can ask your healthcare provider for information that is written for healthcare professionals.

**What else should I know about ADVATE 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 ADVATE 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 ADVATE for a condition for which it is not prescribed. Do not share ADVATE 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 ADVATE. The FDA approved product labeling can be found at [www.ADVATE.com](http://www.ADVATE.com) or 1-877-825-3327. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.


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REFERENCES:

1. ADVATE Prescribing Information.