KOVALTRY®
— The Confidence to Take Control

The only unmodified, full-length rFVIII offering the potential for as few as 2 infusions per week[1]*

***Compared to other rFVIII products**

INDICATION

- KOVALTRY is a medicine used to replace clotting factor (Factor VIII or antihemophilic factor) that is missing in people with hemophilia A.
- KOVALTRY is used to treat and control bleeding in adults and children with hemophilia A. KOVALTRY can reduce the number of bleeding episodes in adults and children with hemophilia A when used regularly (prophylaxis). Your healthcare provider may give you KOVALTRY when you have surgery.
- KOVALTRY is not used to treat von Willebrand Disease.

SELECTED IMPORTANT SAFETY INFORMATION

- You should not use KOVALTRY if you are allergic to rodents (like mice and hamsters) or any ingredients in KOVALTRY.

For additional important risk and use information, please see full Prescribing Information.

Kovaltry®
Antihemophilic Factor (Recombinant)

LEOPOLD I: Main Study

KOVALTRY® Treatment for Adolescents and Adults

In a clinical study, KOVALTRY demonstrated results for **adolescents and adults**[1,2]

LEOPOLD I Study Design:

62 previously treated adolescents and adults (aged 12 to 65 years) with severe hemophilia A were studied for 1 year. Doctors studied bleeds per year, choosing either 2x/week prophylaxis (18 people) or 3x/week prophylaxis (44 people) based on individual needs.

Prophylaxis[1,2]

Throughout the completed study, patients on 2x/week prophylaxis experienced:

1 Bleed per year
(Median Annual Bleed Rate [ABR])
N=18

Patients on 2x/week prophylaxis generally began the study with fewer bleeds and a lower percentage of target joints.

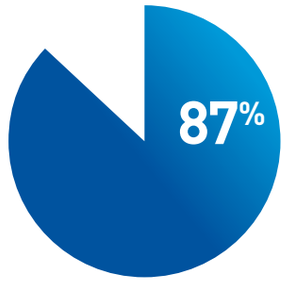
Throughout the completed study, patients on 3x/week prophylaxis experienced:

2 Bleeds per year
(Median Annual Bleed Rate [ABR])
N=44

Patients on 3x/week prophylaxis generally began the study with more bleeds and a higher percentage of target joints.

On Demand[1,2]

When treating on demand,



of bleeds were controlled with 1 or 2 infusions

SELECTED IMPORTANT SAFETY INFORMATION

- Tell your healthcare provider if you have heart disease or are at risk for heart disease.
- The common side effects of KOVALTRY are fever, headache, and rash, in addition to inhibitors in patients who were not previously treated or minimally treated with Factor VIII products.

For additional important risk and use information, please see full Prescribing Information.

Kovaltry®
Antihemophilic Factor (Recombinant)

LEOPOLD I: Main Study

KOVALTRY® Treatment for Adolescents and Adults

In a clinical study, KOVALTRY demonstrated results for **adolescents and adults**[1,2]

Definitions of PK Terms

Area under the curve A measure of the overall amount of a drug in the bloodstream over time after a dose.

Maximum concentration The highest amount of a drug in the blood measured after a dose. For a FVIII treatment, this is sometimes called FVIII level, and is measured in international units per deciliter (IU/dL).

Half-life How much time it takes for the amount of a drug in the blood to decline by one half.

These measures are all related to FVIII levels in the blood over time—from the time that the treatment is infused to the time that it's eliminated from the body.

Chromogenic Substrate Assay[1,2]

Parameter	12 to 17 yrs (N=5)	≥18 yrs (N=21)
Area under the curve (AUC)	1572.0 [IU*h/dL]	2103.4 [IU*h/dL]
Maximum concentration (C_{max})	132.5 [IU/dL]	133.1 [IU/dL]
Half-life ($t_{½}$)	14.4 [h]	14.2 [h]

One-Stage Clotting Assay[1,2]

Parameter	12 to 17 yrs (N=5)	≥18 yrs (N=21)
Area under the curve (AUC)	1013.9 [IU*h/dL]	1601.3 [IU*h/dL]
Maximum concentration (C_{max})	91.7 [IU/dL]	99.7 [IU/dL]
Half-life ($t_{½}$)	11.7 [h]	14.3 [h]

SELECTED IMPORTANT SAFETY INFORMATION

- Your body may make antibodies, called "inhibitors" against KOVALTRY, which may stop KOVALTRY from working properly. If your bleeding is not adequately controlled, it could be due to the development of Factor VIII inhibitors. Consult with your healthcare provider to make sure you are carefully monitored with blood tests for the development of inhibitors to Factor VIII.

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Kovaltry®
Antihemophilic Factor (Recombinant)

LEOPOLD I: Main and Extension Study

KOVALTRY® Treatment for Adolescents and Adults

In a clinical study, KOVALTRY demonstrated results for **adolescents and adults**[1,2,3]

LEOPOLD I Extension Study Design[3]

The extension was an optional continuation of the prophylaxis treatment for up to 12 additional months, during which time patients were treated with KOVALTRY. The extension study aimed to assess the long-term safety and efficacy profile of treatment with KOVALTRY (up to 2 years of treatment in the main and extension period).

Patients aged 12 to 17 years (N=10) and aged ≥18 years (N=52) who completed the 1-year main study period could be enrolled in the extension to collect additional safety and efficacy data.

55

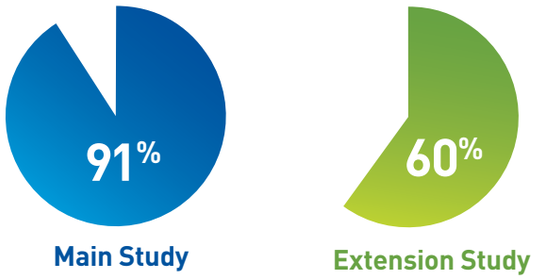
Patients moved from the main study to the extension study*

Of these 55 patients, 8 patients were 12 to 17 years of age and 47 patients were ≥ 18

*43 patients completed the extension study

Efficacy[3]

Median percentage of joint bleeds affecting target joints decreased from main to extension study[3]



Median time to first bleed was prolonged from main to extension study[3]

Median time to first bleed (days)

SELECTED IMPORTANT SAFETY INFORMATION

- Allergic reactions may occur with KOVALTRY. Call your healthcare provider right away and stop treatment if you get tightness of the chest or throat, dizziness, decrease in blood pressure, and nausea.
- Tell your healthcare provider about any side effect that bothers you or that does not go away.
- Call your healthcare provider right away if bleeding is not controlled after using KOVALTRY.

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Kovaltry®
Antihemophilic Factor (Recombinant)

LEOPOLD I: Main and Extension Study

KOVALTRY® Treatment for Adolescents and Adults

In a clinical study, KOVALTRY demonstrated results for **adolescents and adults**[1,2, 3]

Safety[1,2,3]

The common side effects of KOVALTRY are fever, headache and rash in addition to inhibitors in patients who were not previously treated or minimally treated with Factor VIII products.

4	Patients in the main study experienced a drug-related adverse event[1,2]
3	Patients in the extension study experienced a drug-related adverse event[3]
0	Patients in the main study experienced a serious drug-related adverse event[1,2]
1	Patient in the extension study experienced a serious drug-related adverse event[3†]

0 Inhibitors
in all previously treated adolescents and adults in the main and extension studies*

*People with a history of inhibitors or new to FVIII therapy were not included in the trials. People with hemophilia A may develop inhibitors to rFVIII.

†A myocardial infarction occurred in one patient with known risk factors for cardiovascular events. The event was determined not to be related to the specific study drug. The patient recovered after two weeks.

INDICATION

- KOVALTRY is a medicine used to replace clotting factor (Factor VIII or antihemophilic factor) that is missing in people with hemophilia A.
- KOVALTRY is used to treat and control bleeding in adults and children with hemophilia A. KOVALTRY can reduce the number of bleeding episodes in adults and children with hemophilia A when used regularly (prophylaxis). Your healthcare provider may give you KOVALTRY when you have surgery.
- KOVALTRY is not used to treat von Willebrand Disease.

SELECTED IMPORTANT SAFETY INFORMATION

- You should not use KOVALTRY if you are allergic to rodents (like mice and hamsters) or any ingredients in KOVALTRY.

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Kovaltry®
Antihemophilic Factor (Recombinant)

LEOPOLD Kids: Main Study

KOVALTRY® Treatment for Children

In a clinical study, KOVALTRY demonstrated results for **previously treated children**[1,4]

LEOPOLD Kids Part A Study Design:

51 previously treated children (aged 0 to <12 years) with severe hemophilia A were studied for 6 months. Doctors studied bleeds per year, choosing either 2x/week prophylaxis (22 children), or 3x/week or every-other-day prophylaxis (29 children) based on individual needs.

Prophylaxis[1,4]

Within 48 hours after prophylaxis infusion, children experienced:

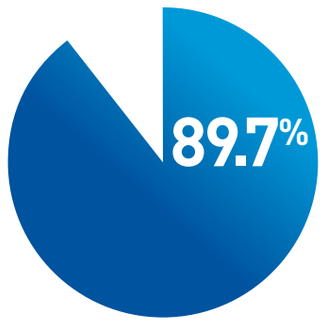
Bleeds per year
(Median ABR)

Throughout the completed study, children experienced:

Bleeds per year
(Median ABR)

On Demand[1,4]

When treating on demand,



of bleeds were controlled with 1 or 2 infusions

SELECTED IMPORTANT SAFETY INFORMATION

- Tell your healthcare provider if you have heart disease or are at risk for heart disease.
- The common side effects of KOVALTRY are fever, headache, and rash, in addition to inhibitors in patients who were not previously treated or minimally treated with Factor VIII products.

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Kovaltry®
Antihemophilic Factor (Recombinant)

LEOPOLD Kids: Main Study

KOVALTRY® Treatment for Children

In a clinical study, KOVALTRY demonstrated results for **previously treated children**[1,4]

Definitions of PK Terms

Area under the curve A measure of the overall amount of a drug in the bloodstream over time after a dose.

Maximum concentration The highest amount of a drug in the blood measured after a dose. For a FVIII treatment, this is sometimes called FVIII level, and is measured in international units per deciliter (IU/dL).

Half-life How much time it takes for the amount of a drug in the blood to decline by one half.

These measures are all related to FVIII levels in the blood over time—from the time that the treatment is infused to the time that it's eliminated from the body.

Chromogenic Substrate Assay[1,4,a]

Parameter	0 to <2 yrs (N=4)	2 to <6 yrs (N=6)	6 to <12 yrs (N=10)[c]
Area under the curve (AUC)	1232.5 [IU*h/dL]	1484.8 [IU*h/dL][b]	1214.5 [IU*h/dL]
Maximum concentration (C_{max})	96.1 [IU/dL]	83.3 [IU/dL][b]	81.6 [IU/dL]
Half-life ($t_{½}$)	9.6 [h]	12.2 [h][b]	12.0 [h]

[a] Only Chromogenic Substrate Assay was used for PK parameter assessment in LEOPOLD Kids.
[b] n=5
[c] One subject considered PK outlier was excluded.

SELECTED IMPORTANT SAFETY INFORMATION

- Your body may make antibodies, called "inhibitors" against KOVALTRY, which may stop KOVALTRY from working properly. If your bleeding is not adequately controlled, it could be due to the development of Factor VIII inhibitors. Consult with your healthcare provider to make sure you are carefully monitored with blood tests for the development of inhibitors to Factor VIII.

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Kovaltry®
Antihemophilic Factor (Recombinant)

LEOPOLD Kids: Main and Extension Study

KOVALTRY® Treatment for Children

In a clinical study, KOVALTRY demonstrated results for **previously treated children**[1,4,5]

LEOPOLD Kids Extension Study Design[5]

The extension was an optional continuation of the prophylaxis treatment for up to 12 additional months, during which time patients were treated with KOVALTRY. The extension study aimed to assess the long-term safety of KOVALTRY in previously treated patients who had been treating with KOVALTRY for 100 accumulated days across the main and extension studies.

Patients ages 0 to <6 years (n=25) and ages 6 to <12 years (n=26) could roll over after reaching at least 50 days of treatment with KOVALTRY, in order to achieve at least 100 cumulative days of treatment with KOVALTRY.

46

Patients moved from the main study to the extension study*

*45 patients completed the extension study

SELECTED IMPORTANT SAFETY INFORMATION

- Allergic reactions may occur with KOVALTRY. Call your healthcare provider right away and stop treatment if you get tightness of the chest or throat, dizziness, decrease in blood pressure, and nausea.
- Tell your healthcare provider about any side effect that bothers you or that does not go away.
- Call your healthcare provider right away if bleeding is not controlled after using KOVALTRY.

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Kovaltry®
Antihemophilic Factor (Recombinant)

LEOPOLD Kids: Main and Extension Study

KOVALTRY® Treatment for Children

In a clinical study, KOVALTRY demonstrated results for **previously treated children**[1,4]

Safety[1,4,5]

The common side effects of KOVALTRY are fever, headache and rash in addition to inhibitors in patients who were not previously treated or minimally treated with Factor VIII products.

1	Patient in the main study experienced a drug-related adverse event[1,4]
1	Patient in the extension study experienced a drug-related adverse event[5]
0	Patients in the main study experienced a serious drug-related adverse event[1,4]
1	Patient in the extension study experienced a serious drug-related adverse event[5]

0 Inhibitors

in all previously treated children in the main and extension studies*†

No confirmed cases of neutralizing antibodies (inhibitors) to FVIII occurred.

*People with a history of inhibitors or new to FVIII therapy were not included in the trials. People with hemophilia A may develop inhibitors to rFVIII.

†One 13-year-old previously treated child tested positive for a low-titer inhibitor. His number of bleeds per year (ABR) was 0 and no change in treatment was required.

INDICATION

- KOVALTRY is a medicine used to replace clotting factor (Factor VIII or antihemophilic factor) that is missing in people with hemophilia A.
- KOVALTRY is used to treat and control bleeding in adults and children with hemophilia A. KOVALTRY can reduce the number of bleeding episodes in adults and children with hemophilia A when used regularly (prophylaxis). Your healthcare provider may give you KOVALTRY when you have surgery.
- KOVALTRY is not used to treat von Willebrand Disease.

SELECTED IMPORTANT SAFETY INFORMATION

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Kovaltry®
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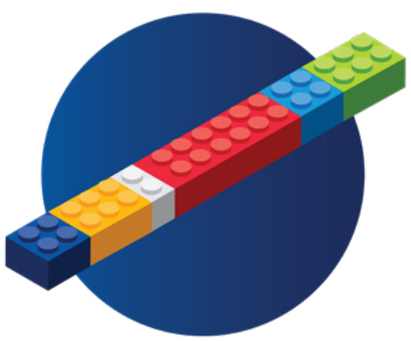
Get to Know KOVALTRY®

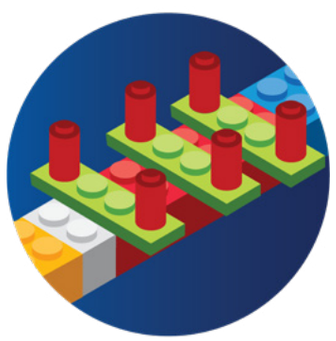
KOVALTRY is designed to stay close to your body's natural FVIII[1]

The Science of KOVALTRY

KOVALTRY is a full-length FVIII treatment. A full-length FVIII treatment has the same 6 sections as natural FVIII. It is also unmodified, meaning no other molecules have been added.[1]



Natural FVIII protein is composed of **6 main sections.** KOVALTRY is full-length because it contains the same 6 sections.[1,6]



When natural FVIII and KOVALTRY are being made, **sugar structures** become attached to them.[1,6]

These sugar structures are then **capped**. Capping protects KOVALTRY from being removed by the body too early. Natural FVIII is also capped in this way.[1,7,8]

Natural FVIII and KOVALTRY both go through a process that prepares them to **attach** to a carrier protein, called von Willebrand factor.[1,9,10]

Von Willebrand factor **carries** KOVALTRY through the bloodstream and keeps it from being broken down. Natural FVIII is also carried through the bloodstream in this way.[1]

SELECTED IMPORTANT SAFETY INFORMATION

- Tell your healthcare provider if you have heart disease or are at risk for heart disease.
- The common side effects of KOVALTRY are fever, headache, and rash, in addition to inhibitors in patients who were not previously treated or minimally treated with Factor VIII products.

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Antihemophilic Factor (Recombinant)

Get to Know KOVALTRY®

KOVALTRY is designed to stay close to your body's natural FVIII[1]

Storage[1]

KOVALTRY can be stored at room temperature (up to 77°F) for up to 1 year

Store KOVALTRY at 36°F to 46°F for up to 30 months from the date of manufacture. Do not freeze. Within this period, KOVALTRY may be stored for a period of up to 12 months at temperatures up to 77°F. Record the starting date of room temperature storage clearly on the unopened product carton. Once stored at room temperature, do not return the product to the refrigerator. The product then expires after storage at room temperature for 12 months, or after the expiration date on the product vial, whichever is earlier. Store vials in their original carton and protect them from extreme exposure to light.

Vial Adapter[1]

KOVALTRY comes with the vial adapter reconstitution kit, which contains:

- 2.5 mL or 5.0 mL prefilled diluent syringe
- Vial adapter with built-in 15-micrometer filter
- 25-gauge butterfly needle

Vial Sizes[1]

KOVALTRY comes in a wide range of vial sizes:

SELECTED IMPORTANT SAFETY INFORMATION

- Your body may make antibodies, called "inhibitors" against KOVALTRY, which may stop KOVALTRY from working properly. If your bleeding is not adequately controlled, it could be due to the development of Factor VIII inhibitors. Consult with your healthcare provider to make sure you are carefully monitored with blood tests for the development of inhibitors to Factor VIII.

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KOVALTRY®
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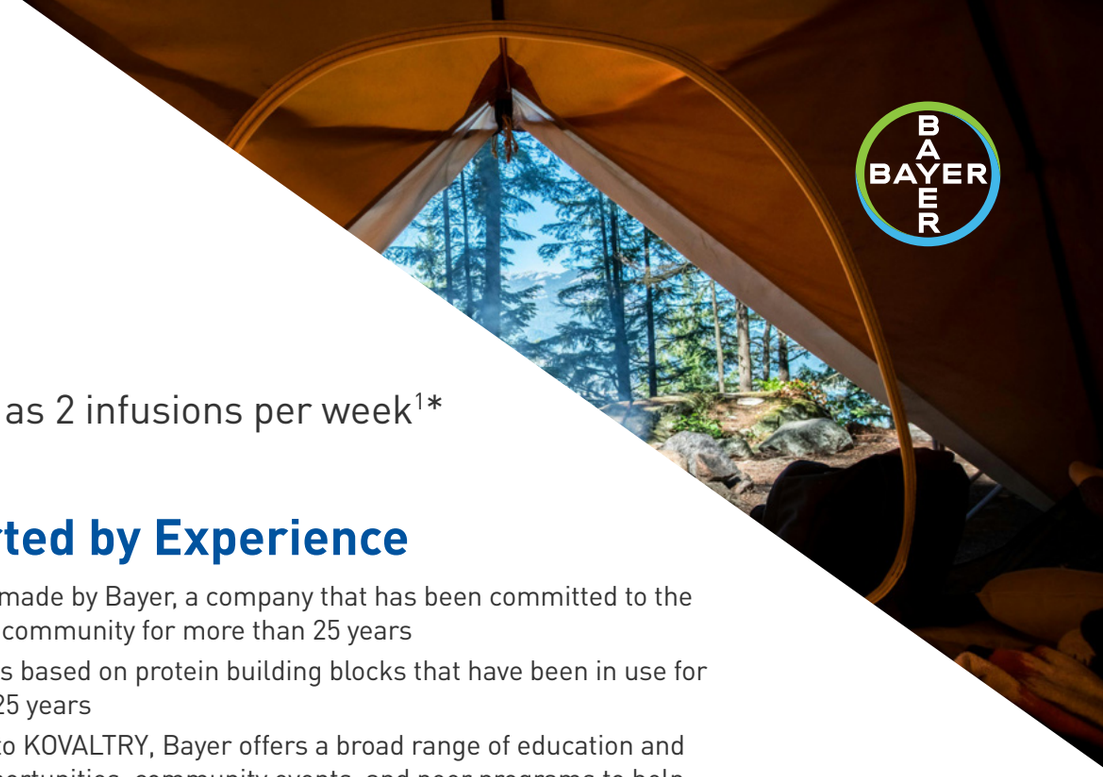

The only unmodified, full-length rFVIII offering the potential for as few as 2 infusions per week[1]*

Dosing[1]

Every person is different: KOVALTRY provides a range of dosing options designed to fit your needs

- Offers the potential for as few as 2 infusions per week[1]

Children	Adolescents and adults
25–50 IU/kg 2x/week, 3x/week, or every other day	20–40 IU/kg 2x/week or 3x/week

Supported by Experience

KOVALTRY is made by Bayer, a company that has been committed to the hemophilia A community for more than 25 years

- KOVALTRY is based on protein building blocks that have been in use for more than 25 years
- In addition to KOVALTRY, Bayer offers a broad range of education and training opportunities, community events, and peer programs to help support people with hemophilia A

Talk to your doctor to see if KOVALTRY is right for you.

*Compared to other rFVIII products

SELECTED IMPORTANT SAFETY INFORMATION

- Allergic reactions may occur with KOVALTRY. Call your healthcare provider right away and stop treatment if you get tightness of the chest or throat, dizziness, decrease in blood pressure, and nausea.
- Tell your healthcare provider about any side effect that bothers you or that does not go away.

References: 1. KOVALTRY [prescribing information]. Whippany, NJ: Bayer HealthCare LLC; 2021. **2.** Saxena K, Lalezari S, Oldenburg J, et al. Efficacy and safety of BAY 81-8973, a full-length recombinant factor VIII: results from the LEOPOLD I trial. Haemophilia. 2016;22(5):706-712. **3.** Bayer Data on File, April 2024. LEOPOLD I Extension. BAY 81-8973. 12594 Extension. Clinical Study Report Addendum 1, PH37225. **4.** Ljung R, Kenet G, Mancuso ME, et al; on behalf of the investigators of the LEOPOLD Kids Trial. BAY 81-8973 safety and efficacy for prophylaxis and treatment of bleeds in previously treated children with severe haemophilia A: results of the LEOPOLD Kids Trial. Haemophilia. 2016;22(3):354-360. **5.** Bayer Data on File, April 2024. LEOPOLD Kids Extension. BAY 81-8973. 13400 Extension. Clinical Study Report, PH-41325. **6.** Pipe SW. Functional roles of the factor VIII B domain. Haemophilia. 2009;15(6):1187-1196. **7.** Lenting PJ, Pegon JN, Christophe OD, Denis CV. Factor VIII and von Willebrand factor—too sweet for their own good. Haemophilia. 2010;16(suppl 5):194-199. **8.** Bovenschen N, Rijken DC, Havekes LM, van Vlijmen BMJ, Mertens K. The B domain of coagulation factor VIII interacts with the asialoglycoprotein receptor. J Thromb Haemost. 2005;3(6):1257-1265. 9.Lenting PJ, van Mourik JA, Mertens K. The life cycle of coagulation factor VIII in view of its structure and function. Blood. 1998;92(11):3983-3996. **10.** Leyte A, van Schijndel HB, Niehrs C,et al. Sulfation of Tyr1680 of human blood coagulation factor VIII is essential for the interaction of factor VIII with von Willebrand factor. J Biol Chem. 1991;266(2):740-746.

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You are encouraged to report negative side effects or quality complaints of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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