Jivi®
antihemophilic factor
(recombinant) PEGylated-aucl

Jivi®– With Them as They Grow

The extended-half life factor VIII treatment with twice weekly dosing for children 7 years of age and older.*

*Please see full **Jivi Prescribing Information** for complete dosing information.

INDICATION

- JIVI is a recombinant DNA-derived, Factor VIII concentrate indicated for use in previously treated adults and pediatric patients 7 years of age and older with hemophilia A (congenital Factor VIII deficiency) for:
  - On-demand treatment and control of bleeding episodes.
  - Perioperative management of bleeding.
  - Routine prophylaxis to reduce the frequency of bleeding episodes.
- Limitations of use
  JIVI is not indicated for use in:
  - Children <7 years of age due to a greater risk for hypersensitivity reactions and/or loss of efficacy.
  - Previously untreated patients (PUPs).
  - Treatment of von Willebrand disease.

SELECTED IMPORTANT SAFETY INFORMATION

- JIVI is contraindicated in patients who have a history of hypersensitivity reactions to the active substance, polyethylene glycol (PEG), mouse or hamster proteins, or other constituents of the product.

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Study Design:

PROTECT Kids and Alfa-PROTECT

PROTECT Kids

A multi-center, prospective, single-arm trial to evaluate the pharmacokinetics, safety and efficacy of Jivi® for prophylaxis and treatment of bleeding in previously treated pediatric patients <12 years of age with severe hemophilia A (n = 73).[1]

Alfa-PROTECT

A multi-center, prospective single-arm study to evaluate the safety of Jivi infusions for prophylaxis and treatment of bleeding in previously treated pediatric patients 7 to <12 years of age with severe hemophilia A (n=35).[1]

Pooled PROTECT Kids and Alfa-PROTECT

The PROTECT Kids and Alfa-PROTECT data were pooled as both studies included participants 7 to <12 years of age. The studies were designed to describe the safety and clinical efficacy of Jivi in previously treated participants 7 to <12 years of age with severe hemophilia A.[1]

Characteristics of Pooled Analysis Set[1]

Children PTPs (7 to <12 years of age)*

57*

ITT population for main efficacy analysis†

42 (prophylaxis twice weekly)‡

Treatment duration (main efficacy period)

26 weeks

*The efficacy of prophylactic treatment was assessed in 57 patients 7 to <12 years of age across PROTECT Kids and Alfa-PROTECT
†ITT: Intention-to-treat
‡15 patients were on an extended interval regimen (every 5 days or every 7 days) in PROTECT Kids, so they are not included in the efficacy data

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- JIVI may contain trace amounts of mouse and hamster proteins. Patients treated with this product may develop hypersensitivity to these non-human mammalian proteins.
- Hypersensitivity reactions may also be related to antibodies against polyethylene glycol (PEG).

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Safety and Tolerability:

PROTECT Kids and Alfa-PROTECT

A demonstrated safety profile in children 7 to <12 years of age

The most common adverse reactions (incidence ≥5%) in clinical trials in previously treated patients (PTPs) ≥7 years of age were headache, fever, cough and abdominal pain.[1]

- There were no study drug-related serious adverse events[2]
- All drug-related events were mild or moderate[2]
- Drug-related AEs: 6.7% (n=4)[2]
- Zero FVIII inhibitors occurred[2]

One pediatric patient developed high titer neutralizing anti-PEG IgM antibodies (titer 1:64) after 2 exposure days associated with low post-infusion FVIII levels and loss of efficacy. Antibodies disappeared after discontinuation and patient restarted treatment with Jivi® 2 months later.[1]

- Three pediatric patients developed low titer and transient anti-PEG IgM antibodies (highest titer 1:4) within the first 4 exposure days resulting in reduction of Jivi recovery (lowest recovery 0.8 kg/dl) in two patients and inconclusive data on recovery in one patient.[1]

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- An immune response associated with IgM anti-PEG antibodies, manifested as symptoms of acute hypersensitivity and/or loss of drug effect, has occurred with JIVI administration. In the clinical trials, the IgM anti-PEG antibodies disappeared within 4-6 weeks. No immunoglobulin class switching from IgM to IgG has been observed.
- A low post-infusion Factor VIII level, in absence of detectable Factor VIII inhibitors, may be due to loss of treatment effect related to high titers of anti-PEG IgM antibodies. In these cases, discontinue JIVI and switch patients to a different anti-hemophilic product.
- A reduced recovery of Factor VIII after start of JIVI treatment may be due to transient low titers of anti-PEG IgM antibodies. In these cases, increase the dose of JIVI until recovery of Factor VIII returns to expected levels.
- The most common (incidence ≥5%) adverse reactions in clinical trials in previously treated patients (PTPs) ≥7 years of age were headache, fever, cough, and abdominal pain.

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Dosing:

PROTECT Kids and Alfa-PROTECT

In the PROTECT Kids and Alfa-PROTECT studies, the median Jivi® prophylaxis dose was 51.7 IU/kg, two times per week.[1]

Children (7 to <12 Years of Age)*,[1] (N=42)

Dosing frequency	2 times per week (25-60 IU/kg)
Median prophylaxis dose/infusion (range)	51.7 IU/kg (22-69 IU/kg)

Jivi approved dosing for children 7 to <12 years of age:
The recommended initial Jivi dosage regimen is 60 IU/kg twice weekly. The patient's dose should be adjusted based on clinical response and/or recovery.[1]

*Pooled patients from PROTECT Kids and Alfa-PROTECT 7 to <12 years of age with at least a 3-month treatment period, modified intention-to-treat (ITT) set

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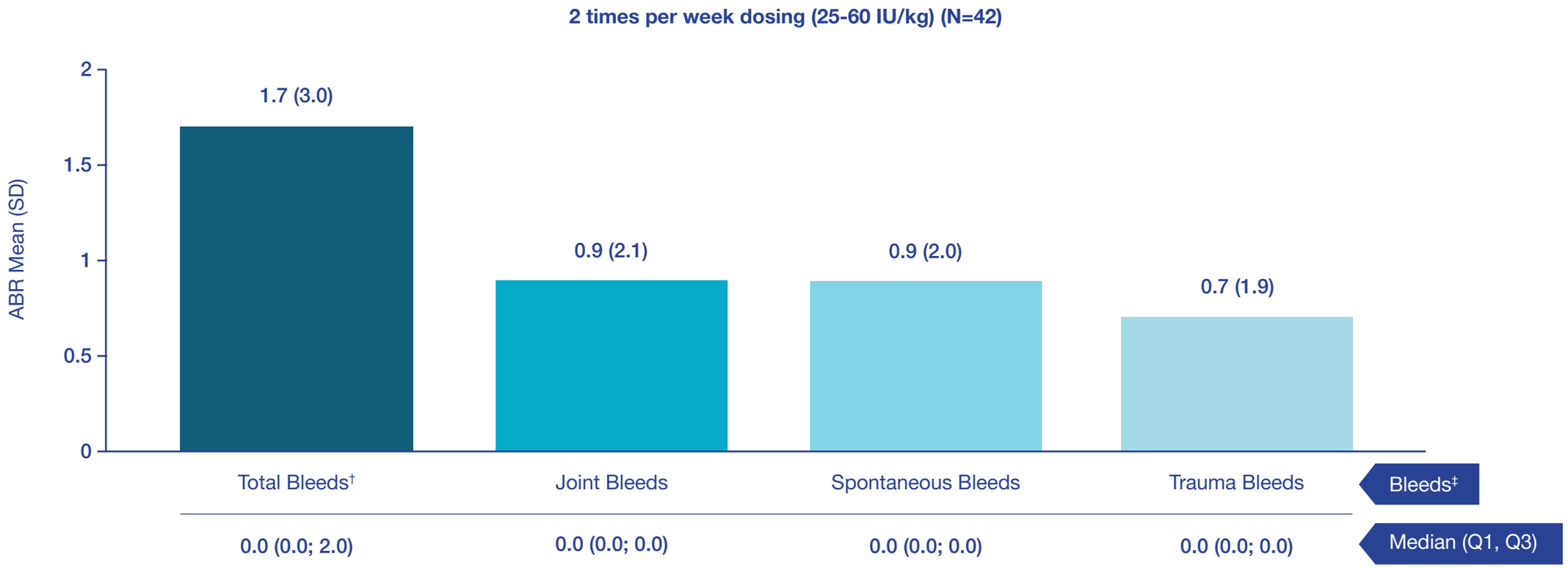
Effective Bleed Protection with Jivi®:

Annualized bleed rates (ABRs)*

In the PROTECT Kids and Alfa-PROTECT studies, ABRs for treated bleeds were assessed for Jivi in patients 7 to <12 years of age as a key secondary endpoint. The median ABR for total bleeds, joint bleeds, spontaneous bleeds and trauma bleeds was zero.[2]



*Modified ITT population included patients with at least a 3-month treatment period
†Total bleeds include spontaneous bleeds, trauma bleeds and joint bleeds
‡Pooled patients from PROTECT Kids and Alfa-PROTECT 7 to <12 years of age, modified ITT set

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- JIVI may contain trace amounts of mouse and hamster proteins. Patients treated with this product may develop hypersensitivity to these non-human mammalian proteins.
- Hypersensitivity reactions may also be related to antibodies against polyethylene glycol (PEG).
- Neutralizing antibody (inhibitor) formation has occurred following administration of JIVI. Carefully monitor patients for development of Factor VIII inhibitors, using appropriate clinical observations and laboratory tests. If expected plasma Factor VIII activity levels are not attained or if bleeding is not controlled as expected with administered dose, suspect the presence of an inhibitor (neutralizing antibody).

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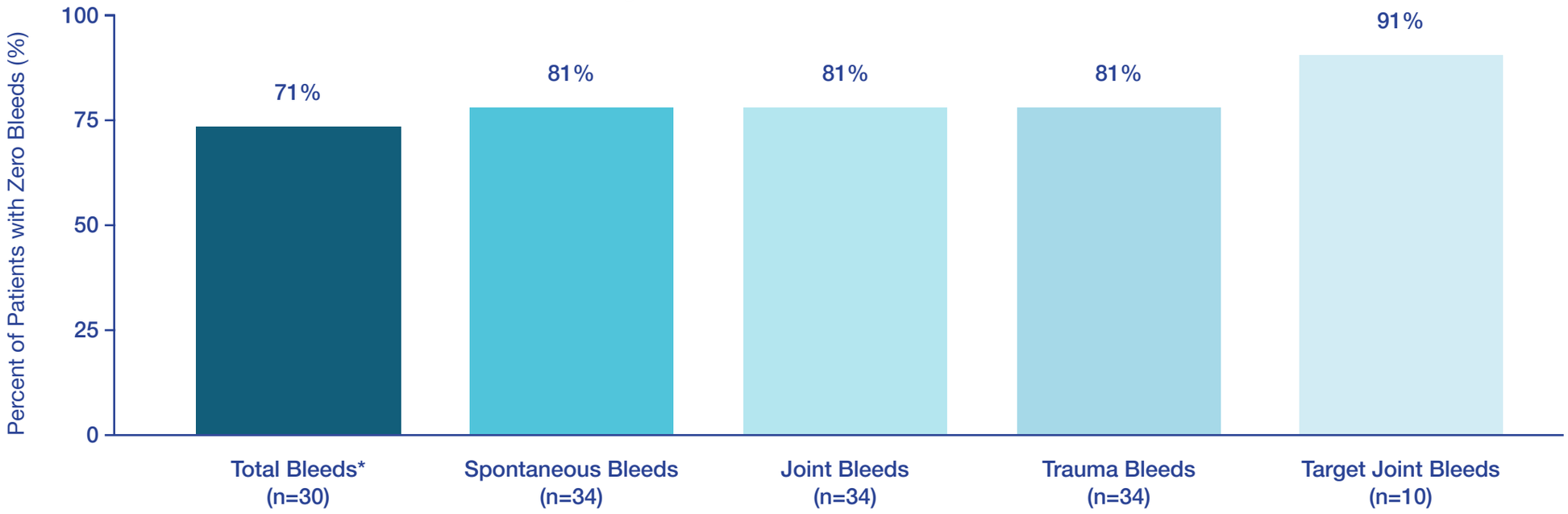
Effective Bleed Protection with Jivi®:

Zero-bleed rates

Percentage of patients with zero bleeds during the entire study period of 26 weeks was 67%.[1] Given variation in patients' treatment start date and exact study phase duration, zero-bleed rate data broken out by bleed type are presented for the last 24 weeks of the 26-week study period.

In the PROTECT Kids and Alfa-PROTECT studies, majority of patients experienced zero treated bleeds, including spontaneous bleeds, joint bleeds, trauma bleeds and target joint bleeds.[2]

Zero-bleed rates during the last 24 weeks of treatment for treated bleeds[2]



*Total bleeds include spontaneous bleeds, trauma bleeds and joint bleeds

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- An immune response associated with IgM anti-PEG antibodies, manifested as symptoms of acute hypersensitivity and/or loss of drug effect, has occurred with JIVI administration. In the clinical trials, the IgM anti-PEG antibodies disappeared within 4-6 weeks. No immunoglobulin class switching from IgM to IgG has been observed.
- A low post-infusion Factor VIII level, in absence of detectable Factor VIII inhibitors, may be due to loss of treatment effect related to high titers of anti-PEG IgM antibodies. In these cases, discontinue JIVI and switch patients to a different anti-hemophilic product.
- A reduced recovery of Factor VIII after start of JIVI treatment may be due to transient low titers of anti-PEG IgM antibodies. In these cases, increase the dose of JIVI until recovery of Factor VIII returns to expected levels.
- The most common (incidence ≥5%) adverse reactions in clinical trials in previously treated patients (PTPs) ≥7 years of age were headache, fever, cough, and abdominal pain.

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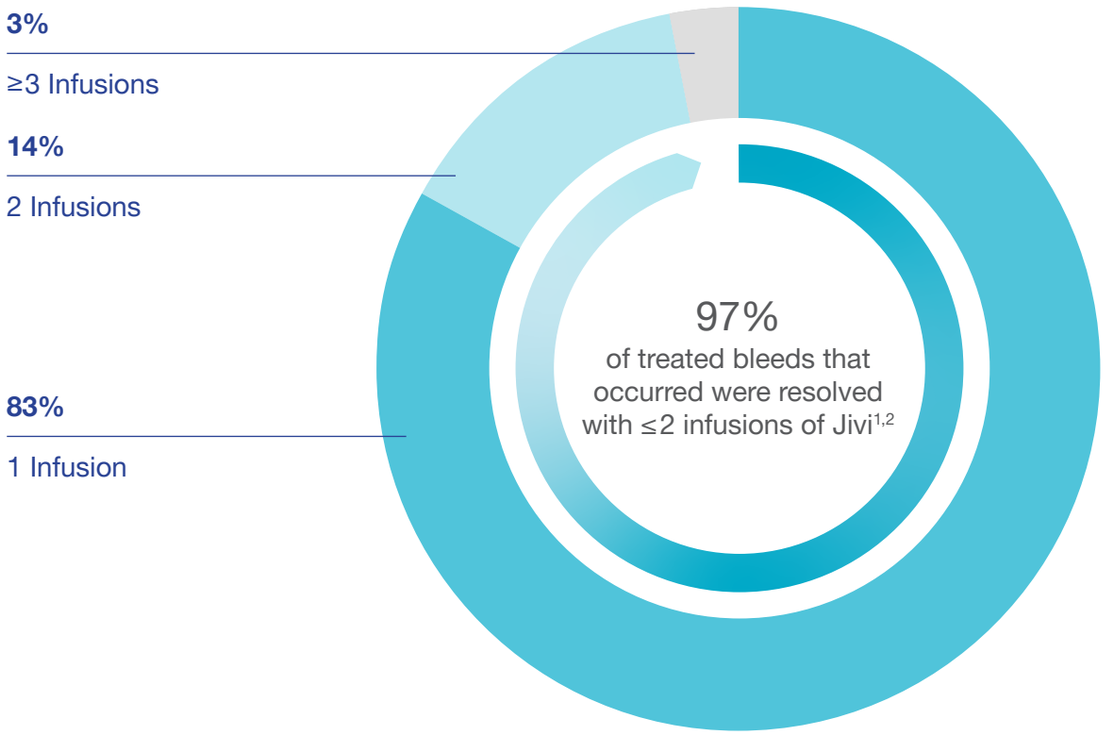
Effective Treatment of Bleeds with Jivi®:

Bleed control

In the PROTECT Kids and Alfa-PROTECT studies, a total of 36 bleeding episodes were treated with Jivi in the 7 to <12 year-old population. 97% of bleeds were successfully treated with one or two infusions. The mean (SD) follow-up time between infusions was one (0.8) day.[1,2]



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Pharmacokinetics (PK):

PK parameters of Jivi®

Chromogenic Substrate Assay[1] 60 IU/kg

PK PARAMETERS (UNIT)	7 TO <12 YEARS OF AGE (n=12)
AUC (IU*h/dL)	2890 ± 547
C_{max} (IU/dL)	130 ± 25.0*
$t_{½}$ (h)	16.0 ± 3.61†
MRT_{IV} (h)	24.1 ± 5.97
V_{SS} (mL/kg)	50.5 ± 9.89
CL (mL/h/kg)	2.14 ± 0.433
Recovery [(IU/dL)/(IU/kg)]	1.93 ± 0.54‡

Results expressed as arithmetic mean ± SD

AUC: area under the curve

C_{max}: maximum drug concentration in plasma after single dose

$t_{½}$: terminal half-life

CL: clearance

MRT_{IV}: mean residence time after an IV administration

V_{SS}: apparent volume distribution at steady-state

*n=13[1]
†n=14[1]
‡Data obtained from all patients' recovery samples, excluding those with anti-drug antibodies, on a twice weekly regimen (n=42) with a range of 1.1-3.8 kg/dL[1]

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Jivi® Is with Your Patient as They Grow:

Dosing in adults and children

Dosing for Children 7 to <12 Years of Age

START SIMPLY	Twice Weekly	**For all prophylaxis patients 7 to <12 years of age:** Recommended starting regimen is Jivi twice weekly (60 IU/kg) Adjust the dose based on the patient's clinical response and/or recovery[1]

Unique Step-Wise Dosing for Patients ≥12 Years of Age

START SIMPLY	Twice Weekly	**For all prophylaxis patients ≥12 years of age:** Recommended starting regimen is Jivi twice weekly (30-40 IU/kg)[1]
ADJUST	Every 5 Days	**Based on bleeding episodes:** Less frequent dosing of Jivi every 5 days (45-60 IU/kg) can be used[1]
FINE-TUNE REGIMEN	⇅	**Based on bleeding episodes:** Dosing frequency may be further adjusted up or down[1]

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Jivi® Reconstitution and Storage:

Vial adapter needleless reconstitution system

The Jivi needleless reconstitution system

- Jivi is available in a range of vial sizes
- Vial adapter with built-in 15-micrometer filter
- 2.5-mL diluent in a 5-mL syringe (500 IU, 1000 IU, 2000 IU and 3000 IU)
- 5.0-mL diluent in a 5-mL syringe (4000 IU only)
- 25-gauge butterfly needle

Jivi is available in a range of vial sizes

Reconstitution with small diluent volumes

Storage

Do not freeze Jivi. Store Jivi at +2°C to +8°C (36°F to 46°F) for up to 24 months from the date of manufacture. Within this period, Jivi may be stored for a period of up to 6 months at temperatures up to +25°C or 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 6 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. Administer reconstituted Jivi as soon as possible. If not, store at room temperature for no longer than 3 hours. Throw away any unused Jivi after the expiration date. Do not use reconstituted Jivi if it is not clear.

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References: 1. Jivi Prescribing Information. May 2025. Bayer. **2.** Data on file. Whippany, NJ: Bayer; 2024. Clinical Study Report B003163.

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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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