The extended-half-life rFVIII with proven protection, safety and unique step-wise dosing[1,2,4,8]

FEEL EMPOWERED
to step up to the challenge with Jivi®

rFVIII, recombinant Factor VIII.

INDICATIONS

- Jivi is an injectable medicine used to replace clotting factor (Factor VIII or antihemophilic factor) that is missing in people with hemophilia A.
- Jivi is used to treat and control bleeding in previously treated adults and adolescents (12 years of age and older) with hemophilia A. Your healthcare provider may also give you Jivi when you have surgery. Jivi can reduce the number of bleeding episodes in adults and adolescents with hemophilia A when used regularly (prophylaxis).
- Jivi is not for use in children below 12 years of age or in previously untreated patients.
- Jivi is not used to treat von Willebrand disease.

SELECTED IMPORTANT SAFETY INFORMATION

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

Please see Important Safety Information throughout, and for additional important risk and use information, please see full Prescribing Information.

Jivi®
antihemophilic factor (recombinant) PEGylated-aucl
LET'S GO

What do you want from your treatment?

Why should you talk to your doctor about Jivi®?

Effective protection
from bleeds

Powerful protection
from bleeds with Jivi®[1]

More time
between infusions

Unique step-wise **dosing schedule** with the potential for fewer infusions with Jivi®[1,2,7]

SELECTED IMPORTANT SAFETY INFORMATION

- Tell your healthcare provider about all of your medical conditions that you have or had.
- Tell your healthcare provider if you have been told that you have inhibitors to Factor VIII.

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What do you want from your treatment?

Why should you talk to your doctor about Jivi®?

Factor VIII levels that
meet my needs

Jivi® **extends the half-life**
of Factor VIII in the body[1*]

A Factor VIII product with
demonstrated **safety**

Up to more than 5 years of
safety data with Jivi®[4,8]

*Half-life is defined as the time it takes for the amount of a drug in the blood to decrease by one half.[3]

SELECTED IMPORTANT SAFETY INFORMATION

- Allergic reactions may occur with Jivi. Call your healthcare provider right away and stop treatment if you get tightness of the chest or throat, dizziness, decrease in blood pressure, or nausea.
- Allergic reactions to polyethylene glycol (PEG), a component of Jivi, are possible.

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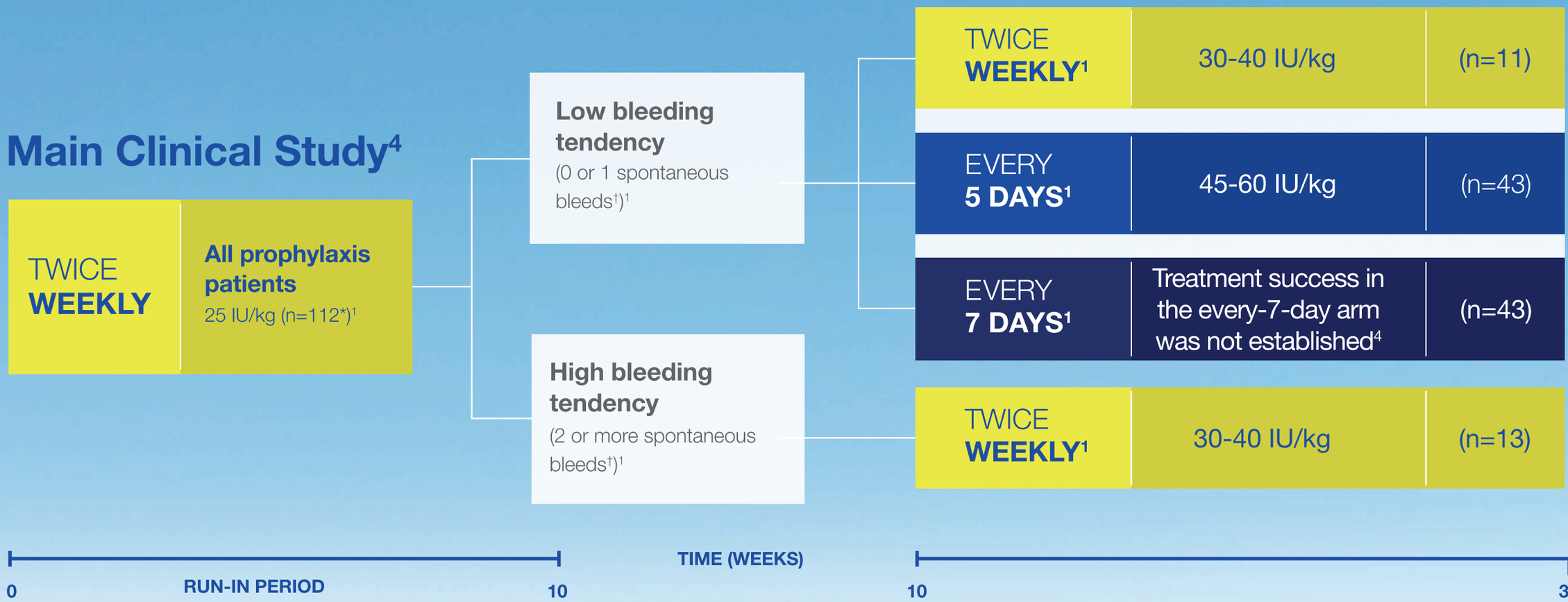
The main clinical study and extension study of Jivi® were designed to reflect real-world treatment[4,8]

Jivi dosing was tailored to patients' bleeding tendencies[4]

Main Clinical Study[4]



IU, international units; kg, kilograms.
*112 patients entered prophylactic treatment arms; an additional 20 patients entered a control arm of on-demand treatment. Two patients in the prophylactic arms left the study prematurely during the run-in period.[1]
†Defined as joint or muscle bleeds and no identified trauma.[1,4]

SELECTED IMPORTANT SAFETY INFORMATION

- Your body can also make antibodies, called "inhibitors," against Jivi, which may stop Jivi from working properly. Consult your healthcare provider to make sure you are carefully monitored with blood tests for the development of inhibitors to Factor VIII.
- If your bleeding is not being controlled with your usual dose of Jivi, consult your doctor immediately. You may have developed Factor VIII inhibitors or antibodies to PEG and your doctor may carry out tests to confirm this.

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Continuously Treated

Up to >5 years[2,4*]

At the end of the main study

97%

of prophylaxis patients opted into the long-term extension study[(1†§)]

Long-term Extension Study[8]

TWICE **WEEKLY**	(n=23) (combined low and high bleeding tendency)
EVERY **5 DAYS**	(n=33)
EVERY **7 DAYS**	(n=23)
VARIABLE **FREQ.¶**	(n=28)

36

UP TO >5 YEARS[2,4*]

†112 patients entered prophylactic treatment arms; an additional 20 patients entered a control arm of on-demand treatment. Two patients in the prophylactic arms left the main study prematurely during the run-in period.[1]
§121 of 134 patients included in the main PROTECT VIII trial continued in the extension study, receiving either on demand treatment (n=14) or prophylaxis (n=107).[8]
¶ Patients who switched dosing frequency at least once after the first week of the extension study were analyzed in a separate variable frequency group.[8]
*As of January 2018 interim analysis.[4,8]

SELECTED IMPORTANT SAFETY INFORMATION

- The common side effects of Jivi are headache, cough, nausea, and fever.
- These are not all the possible side effects with Jivi. Tell your healthcare provider about any side effect that bothers you or that does not go away.

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Effective bleed protection with Jivi® in the main clinical study[1]

	Bleeding Tendency[1]	TOTAL ABR		SPONTANEOUS ABR	
		Median	Mean	Median	Mean
TWICE **WEEKLY**[1]	*LOW**†	1.9	2.2	0	1.2
	*HIGH**‡	4.1	7.2	3.9	3.9
EVERY **5 DAYS**[1]	*LOW*†‖	1.9	3.3	0	1.8

Reduced from 17.4 ABR[1§]

100% of patients **remained** on twice weekly or every 5 days dosing through the end of the main study[1]

88.2% reduction in ABR versus on-demand treatment[1]
ABR, annualized bleed rate.
*n=11; n=13 (twice weekly: low; high).[1]
†Patients with 0 or 1 spontaneous bleed (defined as a joint or muscle bleed and no identified trauma) during weeks 1-10 of the main study.[1,4]
‡Patients with 2 or more spontaneous bleeds (defined as joint or muscle bleeds and no identified trauma) during weeks 1-10 of the main study.[1,4]
§Nine of the 13 subjects in this group were on prior prophylaxis and observed to have a mean number of 17.4 bleeds in the 12 months prior to study entry.[1]
‖n=43 (every 5 days).[1]

INDICATIONS

- Jivi is an injectable medicine used to replace clotting factor (Factor VIII or antihemophilic factor) that is missing in people with hemophilia A.
- Jivi is used to treat and control bleeding in previously treated adults and adolescents (12 years of age and older) with hemophilia A. Your healthcare provider may also give you Jivi when you have surgery. Jivi can reduce the number of bleeding episodes in adults and adolescents with hemophilia A when used regularly (prophylaxis).
- Jivi is not for use in children below 12 years of age or in previously untreated patients.
- Jivi is not used to treat von Willebrand disease.

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ABRs assessed with Jivi® in the long-term extension study[12]

While there were no predetermined efficacy objectives in the extension study, bleeding episodes were documented during the routine course of treatment	TOTAL ABR*		SPONTANEOUS ABR*	
	Median	Mean	Median	Mean
TWICE WEEKLY– LOW AND HIGH BLEEDING TENDENCIES	**1.7**	**3.8**	**0.8**	**2.0**
EVERY 5 DAYS	**1.2**	**3.9**	**0.7**	**2.3**
VARIABLE FREQUENCY‡	**3.1**	**4.8**	**1.8**	**3.1**

*As of 1/31/2018 cut off.[12]
‡Patients who switched dosing frequency at least once after the first week of the extension study were analyzed in a separate variable frequency group.[8]
ABR, annualized bleed rate.

SELECTED IMPORTANT SAFETY INFORMATION

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- Tell your healthcare provider about all of your medical conditions that you have or had.

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Jivi® is an extended-half-life rFVIII with unique step-wise dosing & the potential for fewer infusions[1,2]

Start Simply	TWICE **WEEKLY**	**For all prophylaxis patients:** Recommended starting regimen is Jivi **twice weekly** (30-40 IU/kg)[1]
Step Up	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		**Based on bleeding episodes:** The dosing frequency may be further **adjusted up or down**[1]

8 of 10 patients **reduced** their **dosing frequency** versus the pre-study prophylaxis regimen[5‡]

IU, international units; kg, kilograms; rFVIII, recombinant Factor VIII.
‡40/47 patients in the every-5-day and twice-weekly dosing arms for whom prior prophylaxis dosing records were available.[5]

SELECTED IMPORTANT SAFETY INFORMATION

- Tell your healthcare provider if you have been told that you have inhibitors to Factor VIII.

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Jivi® antihemophilic factor (recombinant) PEGylated-aucl LET'S GO

Jivi® is a PEGylated rFVIII with an extended half-life* of 17.9 hours[1†]

What is Half-life?

Half-life is the time it takes for the amount of a drug in the blood to decrease by one-half.

What is PEGylation used for?

PEGylation increases the amount of time a medicine may stay active in the body (half-life).[6]

PEG, polyethylene glycol; rFVIII, recombinant Factor VIII.
*Half-life is defined as the time it takes for the amount of a drug in the blood to decrease by one half.[3]
†With a single, 60 IU/kg dose.[1]

SELECTED IMPORTANT SAFETY INFORMATION

- Allergic reactions may occur with Jivi. Call your healthcare provider right away and stop treatment if you get tightness of the chest or throat, dizziness, decrease in blood pressure, or nausea.
- Allergic reactions to polyethylene glycol (PEG), a component of Jivi, are possible.

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antihemophilic factor (recombinant) PEGylated-aucl
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Jivi® provided effective treatment of bleeds[1]

83%
1 Infusion

7%
2 Infusions

10%
≥3 Infusions

83%
of prophylaxis patients assessed treatment of bleeds as **“Excellent”** or **“Good”**[1§]

*n=112 on prophylaxis.[1]
†Treatment of bleeds from week 0 through week 36.[1]
‡Two patients discontinued after a single dose of Jivi and were not included in the efficacy analysis.[1]
§On a scale of: Excellent, Good, Moderate, Poor.[1]

SELECTED IMPORTANT SAFETY INFORMATION

- Your body can also make antibodies, called “inhibitors,” against Jivi, which may stop Jivi from working properly. Consult your healthcare provider to make sure you are carefully monitored with blood tests for the development of inhibitors to Factor VIII.
- If your bleeding is not being controlled with your usual dose of Jivi, consult your doctor immediately. You may have developed Factor VIII inhibitors or antibodies to PEG and your doctor may carry out tests to confirm this.

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Target joint resolution with Jivi®[10]

Results from 82 patients who were in the prophylaxis group in the main study and who continued into the extension study.† (median time of 1421 days [range: 700-2071][10])

95%

of **historic target joints*** were resolved[10†]

107 of 113 historic target joints were resolved at time of analysis (data cutoff 8/28/2019)[10]

The median target joint ABR was 0 at the end of the main study and 0 at the extension cutoff date (8/28/2019)[10]

The mean target joint ABR was 1.28 at the end of the main study and 1.06 at the extension cutoff date (8/28/2019)[14]

Analysis consisted of[10]:

- Numbers of historic target joints recorded at study entry
- Numbers of resolved target joints (≤2 spontaneous bleeds during the last 12 months)†

*Patients remaining on the same prophylaxis regimen during the last 90 days of treatment. Median joint ABRs were 0.00 for twice-weekly and 0.00 for every-5-day dosing interval.[11]
† As defined by the International Society of Thrombosis and Hemostasis (ISTH).[10]

SELECTED IMPORTANT SAFETY INFORMATION

- The common side effects of Jivi are headache, cough, nausea, and fever.
- These are not all the possible side effects with Jivi. Tell your healthcare provider about any side effect that bothers you or that does not go away.

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Jivi®
antihemophilic factor (recombinant) PEGylated-aucl
LET'S GO

Target joint resolution with Jivi®[10]

Results from 82 patients who were in the prophylaxis group in the main study and who continued into the extension study.† (median time of 1421 days [range: 700-2071][10])

91%

of **historic or new target joints*** were resolved[10†]

111 of 122 historic or new target joints were resolved at time of analysis (data cutoff 8/28/2019)[10]

The median target joint ABR was 0 at the end of the main study and 0 at the extension cutoff date (8/28/2019)[10]

The mean target joint ABR was 1.28 at the end of the main study and 1.06 at the extension cutoff date (8/28/2019)[14]

Analysis consisted of[10]:

- Numbers of historic target joints, as judged by the investigator, recorded at study entry
- Numbers of new target joints that developed on-study (≥3 spontaneous bleeds within 6 months)†
- Numbers of resolved target joints (≤2 spontaneous bleeds during last 12 months)†

*Patients remaining on the same prophylaxis regimen during the last 90 days of treatment. Median joint ABRs were 0.00 for twice-weekly and 0.00 for every-5-day dosing interval.[11]
† As defined by the International Society of Thrombosis and Hemostasis (ISTH).[10]

INDICATIONS

- Jivi is an injectable medicine used to replace clotting factor (Factor VIII or antihemophilic factor) that is missing in people with hemophilia A.
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- Jivi is not used to treat von Willebrand disease.

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Long-term safety data with Jivi® in adolescents and adults[1,2,4]

0 Factor VIII inhibitors[1]	No confirmed cases of inhibitors against **Factor VIII** occurred.*
2/134 patients[1,4]	Allergic reactions occurred in 2 patients. In 1 patient, the allergic reaction was related to **polyethylene glycol (PEG)**, a component of Jivi.
4 most common side effects[1†]	Headache, Cough, Nausea, Fever
2 patients (1.7%)[8]	Serious drug-related adverse events occurred in 2 patients.
No increasing plasma PEG levels over time[8,13,‡]	Our bodies have known mechanisms for removing PEG. It is excreted through the kidney (via urine) and liver (via feces).

Jivi is indicated for previously treated adolescents and adults aged 12 years and older with hemophilia A.[1]

*A Factor VIII inhibitor (1.7 BU/mL) was reported in one previously treated adult subject. Repeat testing did not confirm the presence of a Factor VIII inhibitor (BU, Bethesda units; mL, milliliters).[1]

†In at least 5% of patients.[1]

‡As of January 2018 interim analysis.

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Up to more than 5 years of safety data in previously treated patients 12 years of age and older[2,4]

SELECTED IMPORTANT SAFETY INFORMATION

- Tell your healthcare provider if you have been told that you have inhibitors to Factor VIII.

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Jivi® needleless reconstitution system and storage[1]

The Jivi® needleless reconstitution system contains[1]:

- Vial adapter with built-in 15-micrometer filter
- 2.5-mL diluent in a 5-mL syringe
- 25-gauge butterfly needle

Storage at room temperature (up to 77°F) for up to 6 months[1]

Store Jivi at 36°F to 46°F for up to 24 months from the date of manufacture. Do not freeze. Within this period, Jivi may be stored for a single period of up to 6 months at temperatures up to 77°F. Record the starting date of room-temperature storage on the unopened product carton. Once stored at room temperature, do not return the product to the refrigerator. The shelf life then expires after storage at room temperature for 6 months, or after the expiration date on the product vial, whichever is earlier. Do not use Jivi after the expiration date indicated on the vial. Protect Jivi from extreme exposure to light and store the vial with the lyophilized powder in the carton prior to use.

Jivi is available in a range of vial sizes[1]

Reconstitution with small diluent volumes

IU, international units; mL, milliliters.

SELECTED IMPORTANT SAFETY INFORMATION

- Allergic reactions may occur with Jivi. Call your healthcare provider right away and stop treatment if you get tightness of the chest or throat, dizziness, decrease in blood pressure, or nausea.

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Feel empowered to step up to the challenge with Jivi®

The extended-half-life rFVIII with proven protection, safety and unique step-wise dosing[1,2,4,8]

Powerful protection with Jivi® from bleeds[1]

Up to more than 5 years of safety data[2,4]

Potential for fewer infusions with Jivi® with a twice-weekly starting dose and the potential to step up every 5 days, and fine tune[1]

Extended half-life with Jivi®: Jivi stays in the body longer, with a half-life of 17.9 hours[1*†]

		For patients ≥ 12 years
Start Simply	TWICE **WEEKLY**	**For all prophylaxis patients:** Recommended starting regimen is Jivi **twice weekly** (30-40 IU/kg)[1]
Step Up	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	⇅	**Based on bleeding episodes:** The dosing frequency may be further **adjusted up or down**[1]

IU, international units; kg, kilograms; rFVIII, recombinant Factor VIII.
*Half-life is defined as the time it takes for the amount of a drug in the blood to decrease by one half.[3]
†With a single, 60 IU/kg dose.[1]

SELECTED IMPORTANT SAFETY INFORMATION

- Allergic reactions to polyethylene glycol (PEG), a component of Jivi, are possible.

References: 1. Jivi® Prescribing Information. Whippany, NJ: Bayer LLC; 2018. **2.** Data on file. Tx Review 0918. Bayer; 2018. **3.** Ratain MJ, Plunkett WK Jr. Principles of pharmacokinetics. In: Kufe DW, Pollock RE, Weichselbaum RR, et al, eds. *Holland-Frei Cancer Medicine*. 6th ed. Hamilton, Ontario: BC Decker; 2003. **4.** Reding MT, Ng HJ, Poulsen LH, et al. Safety and efficacy of BAY 94-9027, a prolonged-half-life factor VIII. *J Thromb Haemost*. 2017;15(3):411-419. **5.** Kerlin BA, Simpson ML, Reding MT, Linardi C, Schwartz L. Comparison of bleeding rates before and during BAY 94-9027 prophylaxis: data from the PROTECT VIII study and extension. Presented at: 4th Biennial Summit of the Thrombosis & Hemostasis Societies of North America; March 8-10, 2018; San Diego, CA. **6.** Veronese FM, Mero A. The impact of PEGylation on biological therapies. *BioDrugs*. 2008;22(5):315-329. **7.** Data on file. CSR 38453. Bayer; 2020. **8.** Lalezari S et al. Haemophilia 2019;25:1011-1019. **9.** CSRs [main study, extension study] **10.** Reding MT et al. Haemophilia. 2020;26(4):e201-e204. **11.** Reding M et al. Poster P29. Presented at the Hemostasis and Thrombosis Research Society 2019 Scientific Symposium. 9–11 May 2019, New Orleans, Louisiana. **12.** Data on file. Jivi PROTECT VIII Extension JAN 2018 CSR ABR data. **13.** Data on file. CSR 2.5. Bayer, 2018. **14.** Data on file. Jivi PROTECT VIII Extension AUG 2019 CSR Target Joint Analysis data; Bayer.

Ask your healthcare professional if Jivi® is right for you.

Please see Important Safety Information throughout, and for additional important risk and use information, please see full Prescribing Information.

You are encouraged to report 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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