For your patients 12 years of age or older with Hemophilia A

Recommend the coverage of Jivi®

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.

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

Jivi®
antihemophilic factor (recombinant) PEGylated-aucl

Explore dosing and...

Dosing with Jivi® for routine prophylaxis

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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- Hypersensitivity reactions, including severe allergic reactions, have occurred with JIVI. Monitor patients for hypersensitivity symptoms. Early signs of hypersensitivity reactions, which can progress to anaphylaxis, may include chest or throat tightness, dizziness, mild hypotension and nausea. If hypersensitivity reactions occur, immediately discontinue administration and initiate appropriate treatment.
- JIVI may contain trace amounts of mouse and hamster proteins. Patients treated with this product may develop hypersensitivity to these non-human mammalian proteins.

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...PK parameters of Jivi® in patients ≥12 years of age[1]

PK parameters of Jivi® in the PROTECT VIII trial (arithmetic mean ± SD)[1]

- Measured following a single dose (25 IU/kg and 60 IU/kg)[1]

	Chromogenic assay		One-stage assay	
PK parameters (unit)	25 IU/kg n=7	60 IU/kg* n=29	25 IU/kg n=7	60 IU/kg* n=29
AUC (IU*h/dL)	1640 ± 550	4060 ± 1420	1640 ± 660	4150 ± 1060
C_{max} (IU/dL)	64.2 ± 9.2	167 ± 30	69.4 ± 11.3	213 ± 71
$t_{½}$ (h)	18.6 ± 4.6	17.9 ± 4.0	21.4 ± 13.1	17.4 ± 3.8
MRT_{IV} (h)	26.7 ± 6.6	25.8 ± 5.9	29.0 ± 14.0	24.5 ± 5.4
V_{ss} (mL/kg)	42.8 ± 5.0	39.4 ± 6.3	44.7 ± 5.4	36.0 ± 6.5
CL (mL/h)	142 ± 33	121 ± 53	146 ± 44	114 ± 41
CL (mL/h/kg)	1.68 ± 0.39	1.63 ± 0.52	1.74 ± 0.54	1.52 ± 0.38
Recovery [(IU/dL)/(IU/kg)]	2.13 ± 0.47	2.53 ± 0.43†	2.21 ± 0.55	3.25 ± 0.84†

AUC, area under the curve; C_{max}, maximum drug concentration in plasma after single dose; CL, clearance; MRT_{IV}, mean residence time after an IV administration; PK, pharmacokinetic; SD, standard deviation; $t_{1/2}$, terminal half-life; V_{ss}, apparent volume distribution at steady-state.

*Combined data from phase 1 and phase 2/3 studies.
†Recovery value could not be calculated for one subject.

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- 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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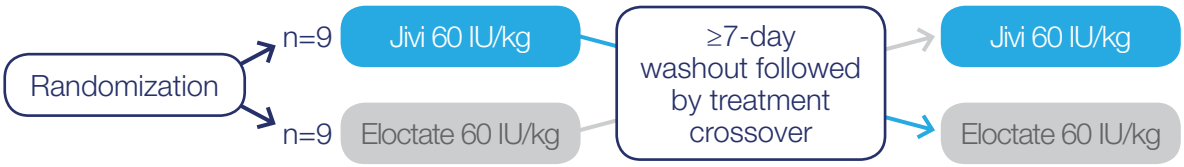
Crossover study examining PK characteristics of Jivi® and Eloctate® (N=18)[2]*

Study description	The PK profiles of Jivi® and Eloctate® were compared in a randomized, open-label, single-dose, crossover study with a washout period between. • Previously treated male patients aged 18-65 years with severe hemophilia A with no history of FVIII inhibitors • Primary endpoint: $AUC_{(0\text{-}t_{last})}$† based on one-stage clotting assay

Dosing



PK assessment	PK samples were collected predose, and at 11 time points: 0.25, 0.5, 1, 3, 6, 8, 24, 48, 72, 96, and 120 hours after infusion.

AUC, area under the curve (from time zero to last data point)†; PK, pharmacokinetic.

*Adapted from Shah et al.

†Area under the curve is the total amount of a drug that reaches the bloodstream, measured by plasma concentration, over time.[3]

SELECTED IMPORTANT SAFETY INFORMATION

- 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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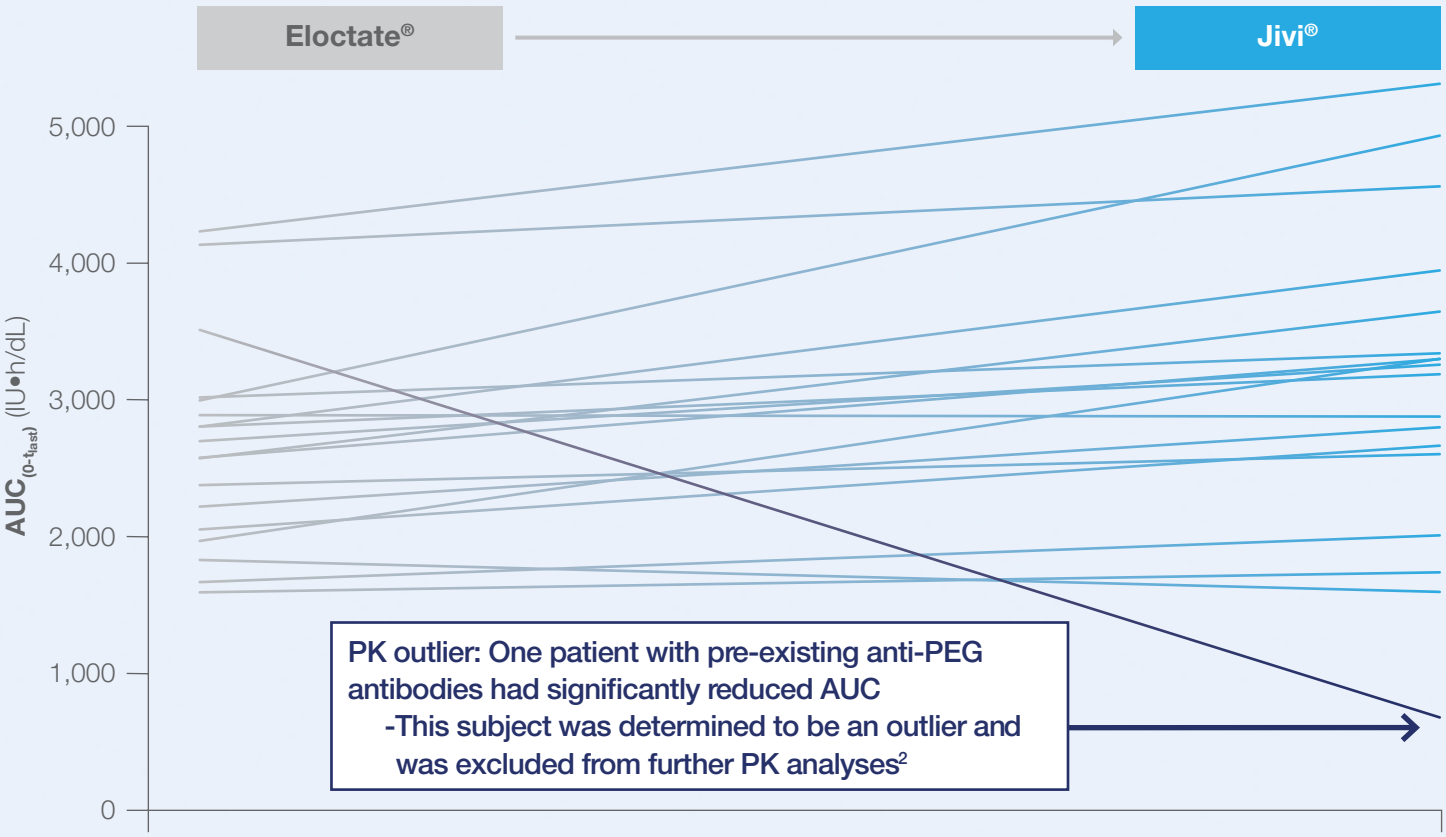
Jivi® AUC compared to Eloctate® in 18 patients[2]*



- The pre-specified criteria for non-inferiority of Jivi® vs Eloctate® were met
- Superiority criteria of the Jivi®:Eloctate® ratio were not met (95% CI 0.84–1.46; *P*=0.46)

PEG, polyethylene glycol.

*Adapted from Shah et al.

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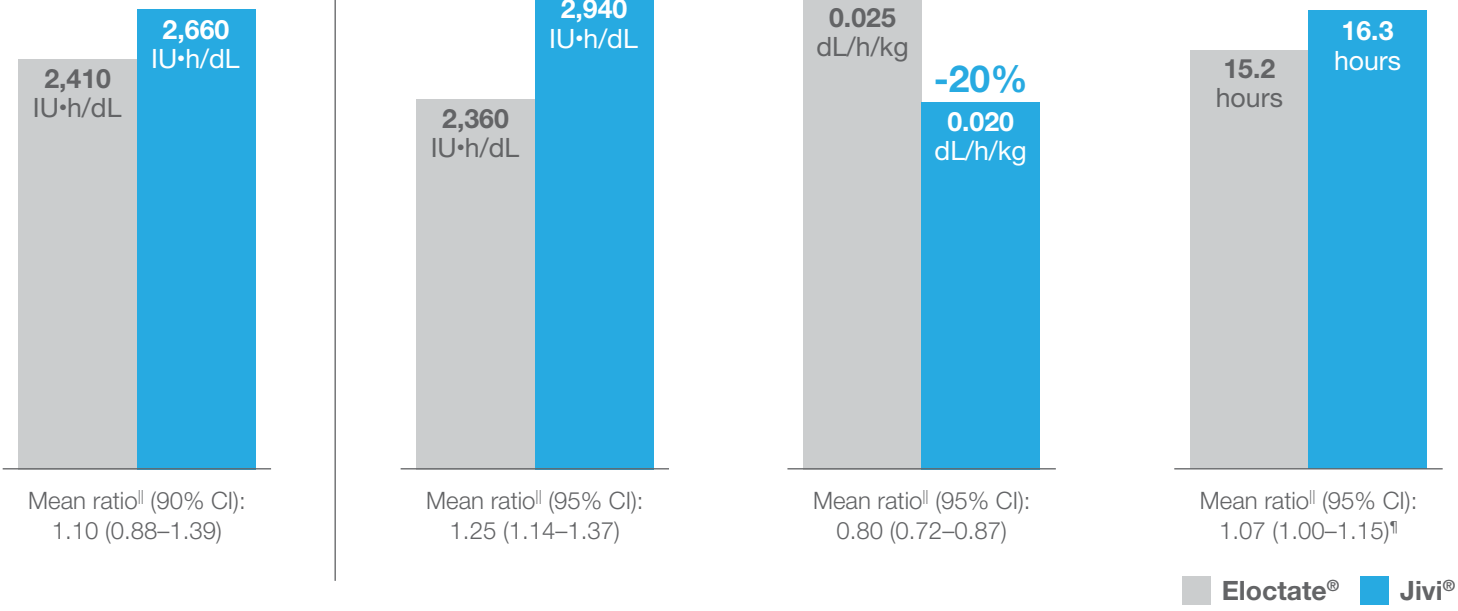
Comparative PK results for Jivi® vs Eloctate®[2]

Compared with Eloctate, Jivi demonstrated statistically significantly (N=17)*:



AUC, area under the curve (from time zero to last data point); CI, confidence interval; PK, pharmacokinetic.

*Excluding outlier patient, who had anti-PEG antibodies.[2]
†Area under the curve is the total amount of a drug that reaches the bloodstream, measured by plasma concentration over time.[3]
‡Clearance is the time it takes for a drug to be completely eliminated from the body.[4]
§Half-life is the time it takes for the amount of a drug in the blood to decrease by one half.[5]
‖Geometric least squares.[2]
¶Actual 95% confidence interval is 1.0026 - 1.1516.[6]

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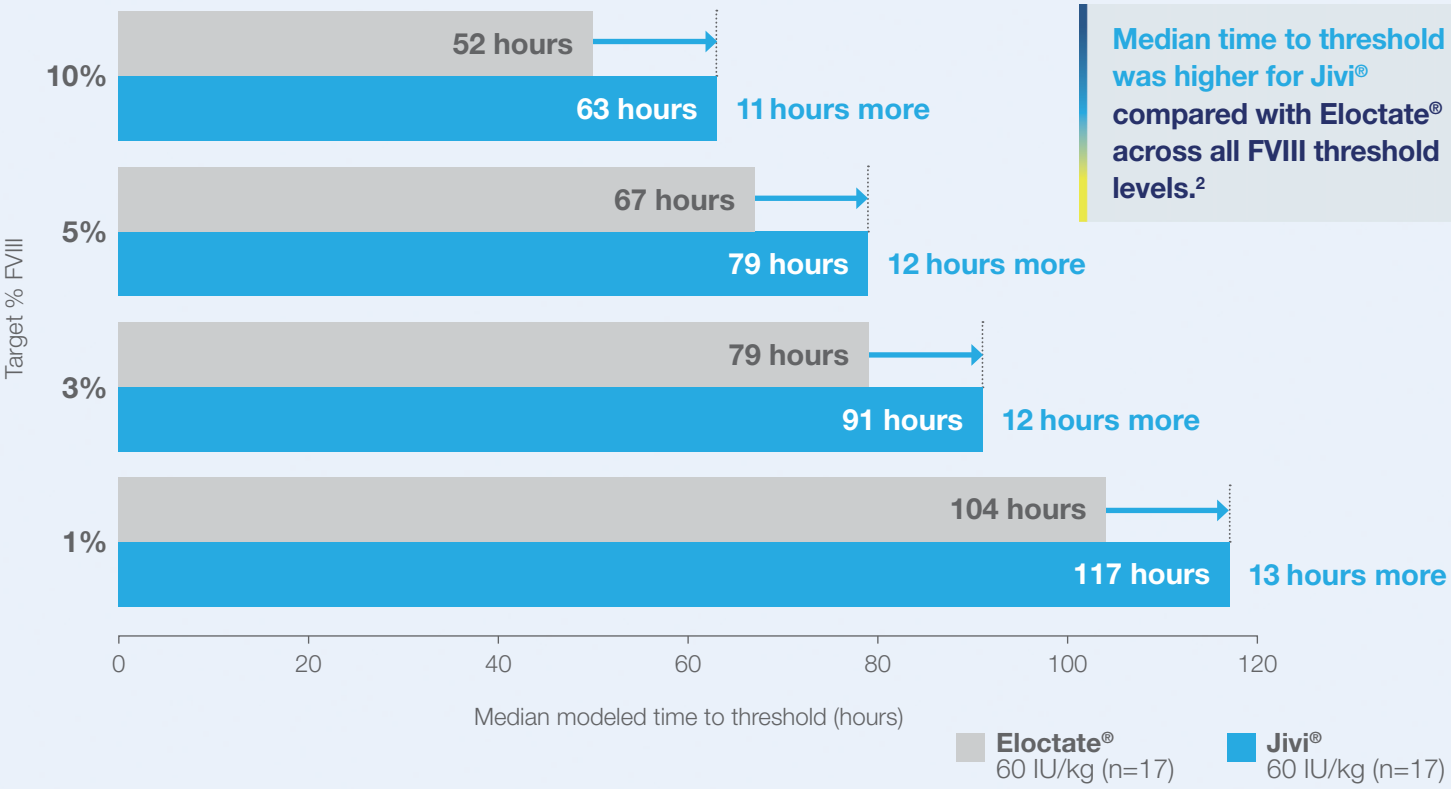
Median time to target FVIII threshold levels with Jivi® vs Eloctate®[2]

Estimated from a population PK model (excluding outlier, N=17)[2]*



Median time to threshold was higher for Jivi® compared with Eloctate® across all FVIII threshold levels.[2]

PK, pharmacokinetic.

*Adapted from Shah et al. A population PK model was developed based on data obtained by a one-stage assay to simulate time to reach FVIII thresholds of 1, 3, 5, and 10% FVIII.[2]

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Compared with Eloctate®, Jivi® demonstrated statistically significantly (N=17)*:

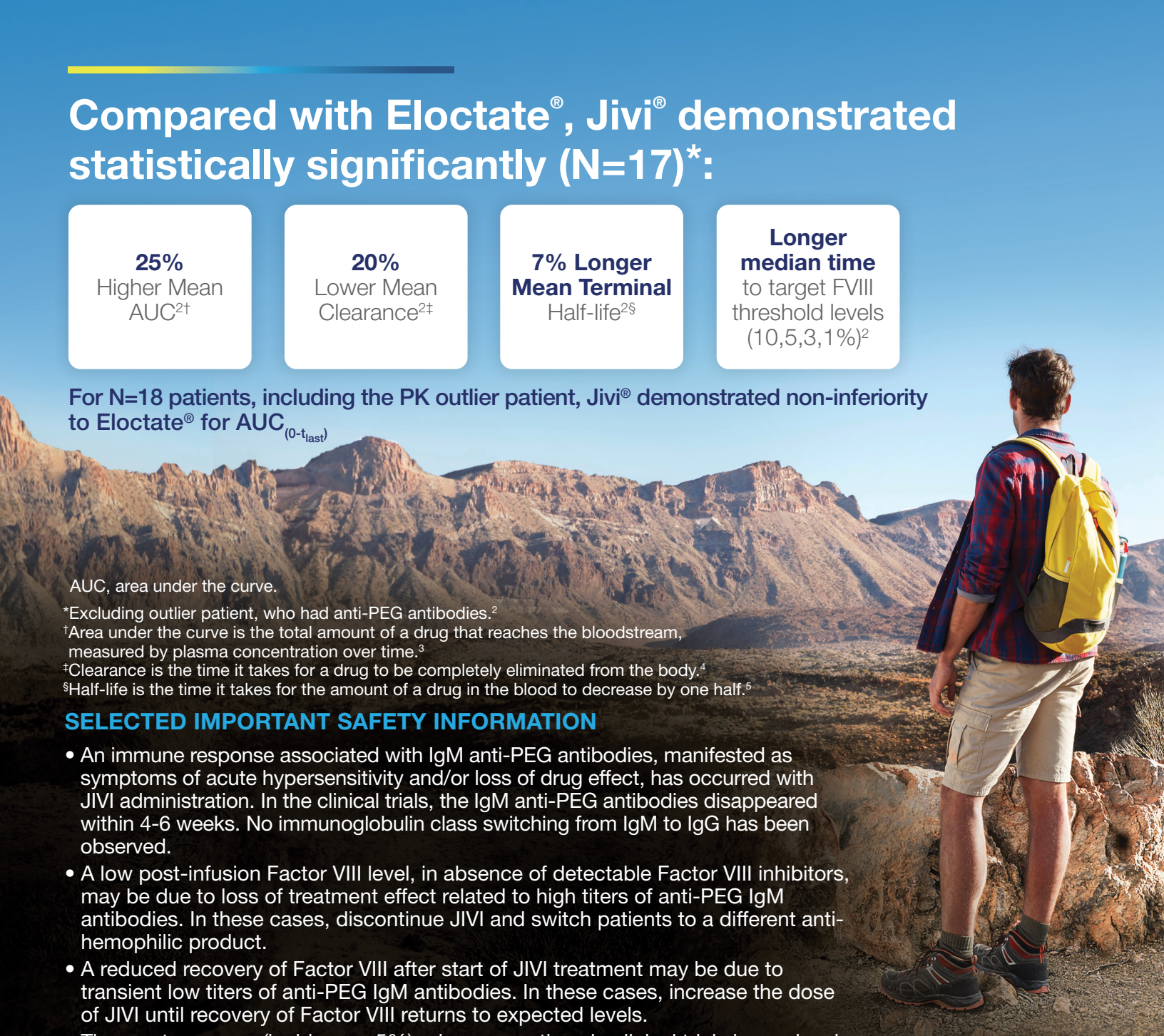
25%
Higher Mean AUC[2†]

20%
Lower Mean Clearance[2‡]

7% Longer Mean Terminal
Half-life[2§]

Longer median time
to target FVIII threshold levels (10,5,3,1%)[2]

For N=18 patients, including the PK outlier patient, Jivi® demonstrated non-inferiority to Eloctate® for $AUC_{(0\text{-}t_{last})}$



AUC, area under the curve.

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References: 1. Jivi® Prescribing Information. Whippany, NJ: Bayer LLC; May 2025. **2.** Shah A, Solms A, Wiegmann S, et al. Direct comparison of two extended-half-life recombinant FVIII products: a randomized, crossover pharmacokinetic study in patients with severe hemophilia A. *Ann Hematol*. 2019;98(9):2035-2044. doi:10.1007/s00277-019-03747-2. **3.** Anderson PL. The ABCs of pharmacokinetics. HealthCentral Corporation. Accessed May 6, 2025. http://www.thebody.com/content/art875.html. **4.** Dhillon S, Gill K. Basic pharmacokinetics. In: Dhillon S, Kostrzewski A, eds. *Clinical Pharmacokinetics*. London, UK: Pharmaceutical Press; 2006. **5.** 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. **6.** Jivi vs Eloctate PK Confidence Interval Data Table from CSR. Bayer; 2019.

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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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