



For patients 12 years of age or older
with Hemophilia A

Consider the pharmacokinetic coverage of Jivi®

Pharmacokinetics is the study of the activity of drugs in the body over a period of time.

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.
- 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.

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


antihemophilic factor
(recombinant) PEGylated-auct
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How do I take Jivi®?

Jivi® is an extended-half-life rFVIII with unique step-wise dosing

Start simply	TWICE WEEKLY	For all prophylaxis patients: Recommended starting regimen is Jivi twice weekly (30-40 IU/kg)
Step up	EVERY 5 DAYS	Based on bleeding episodes: Less frequent dosing of Jivi every 5 days (45-60 IU/kg) can be used
Fine tune		Based on bleeding episodes: The dosing frequency may be further adjusted up or down

Ask your doctor if Jivi® is right for you.

Key term:
Factor VIII is a protein in the blood that is responsible for clotting. It is missing in patients with hemophilia A.

IU, international units; kg, kilograms; rFVIII, recombinant Factor VIII.

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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Jivi[®] rFVIII levels remain elevated and sustained over time

- The pharmacokinetics (PK) of Jivi[®] were investigated in 29 severe hemophilia A patients (≥12 years of age) following a single 60 IU/kg dose (measured by chromogenic assay)
- PK is the activity of drugs in the body over a period of time

PK was primarily measured by*

- ✓ **Clearance**—the speed at which a drug is removed from the body[†]
- ✓ **Area under the curve**—the total amount of a drug that reaches the bloodstream, measured by plasma concentration, over time[‡]
- ✓ **Half-life**—the amount of time that it takes for the concentration of a drug to be reduced by half and is used to determine how long a drug remains active in the body

Jivi[®] demonstrated a half-life of 17.9 hours.[§]

rFVIII, recombinant Factor VIII.

*Other PK parameters measured were maximum drug concentration in plasma after a single dose, mean residence time after an IV administration, and apparent volume distribution at steady-state.

[†]Clearance measured 1.63 mL/h/kg.

[‡]Area under the curve measured 4060 IU*^h/dL.

[§]With a single, 60 IU/kg dose (IU, international units; kg, kilograms).

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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Jivi[®] vs Eloctate[®] PK comparison

How Jivi[®] and Eloctate[®] were compared

- ✓ Jivi[®] and Eloctate[®] compared PK parameters in a **crossover study** of 18 male patients aged 18-65 with severe hemophilia A. Patients were each given a single dose of either Jivi[®] or Eloctate[®], then halfway through the study, following a washout, patients switched to a single dose of the other treatment
- ✓ **One patient with preexisting anti-PEG antibodies had significantly different PK results.** This patient was determined to be an outlier. Including this outlier patient in the analysis (N=18), there were no PK differences observed. This outlier patient was excluded from further analysis
- ✓ In the **17 patients** (excluding the outlier), there were **3 statistically significant PK differences:**

Compared with Eloctate[®]

Jivi[®] gave patients a
**HIGHER
AMOUNT**
of medication available
for clotting over time*

Jivi[®]
**REMAINED
LONGER**
in the body[†]

Jivi[®] had a
**LONGER
HALF-LIFE[‡]**

PK, pharmacokinetics; FVIII, factor VIII.

*Jivi[®] had a higher mean area under the curve (+25%).

†Jivi[®] had lower mean clearance (-20%).

‡Jivi[®] had a longer mean half-life (7%).

SELECTED IMPORTANT SAFETY INFORMATION

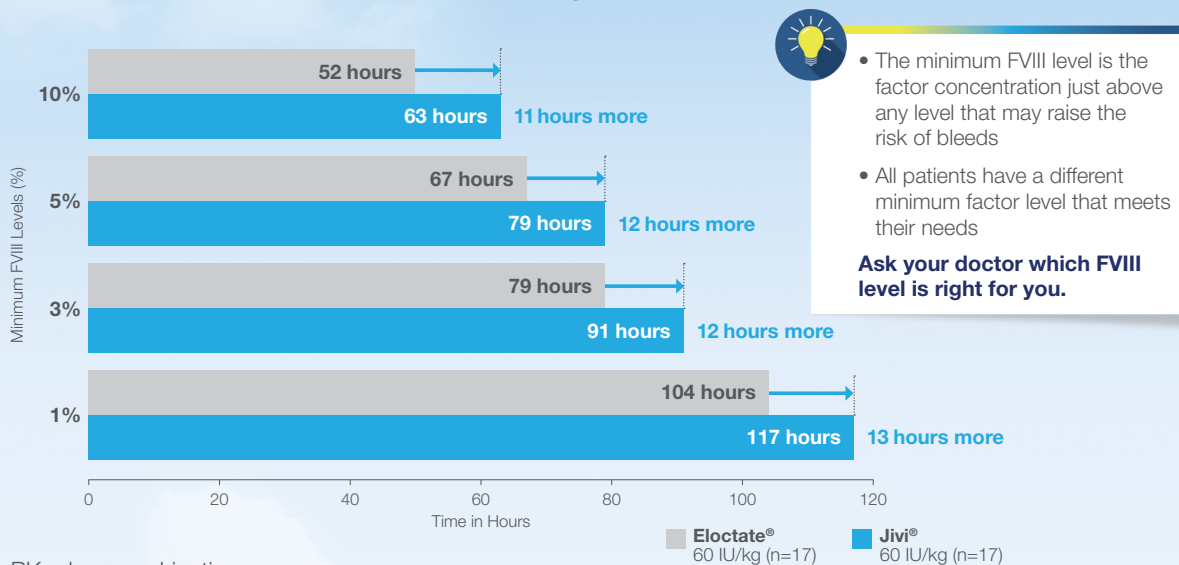
- The common side effects of Jivi are headache, cough, nausea, and fever.
- These are not all the possible side effects with Jivi. Tell your healthcare provider about any side effect that bothers you or that does not go away.

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Jivi[®] demonstrated more time before reaching minimum FVIII levels

Jivi[®] median time to minimum FVIII levels (compared to Eloctate[®]) in a population PK analysis (excluding the outlier patient, N=17)[§]



- The minimum FVIII level is the factor concentration just above any level that may raise the risk of bleeds
- All patients have a different minimum factor level that meets their needs

Ask your doctor which FVIII level is right for you.

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

HIGHER AMOUNT

of medication available for clotting over time*

REMAINED LONGER

in the body[†]

LONGER HALF-LIFE[‡]

MORE TIME

before reaching minimum FVIII levels[§]

For N=18 patients, including the PK outlier patient, Jivi[®] demonstrated noninferiority to Eloctate[®] for AUC_(0-t last).

Ask your doctor if the pharmacokinetic coverage of Jivi[®] is right for you.

PK, pharmacokinetics; FVIII, factor VIII.

*Jivi[®] had a higher mean area under the curve (+25%).

†Jivi[®] had lower mean clearance (-20%).

‡Jivi[®] had a longer mean half-life (7%).

§10%: 63 hours on Jivi[®] vs 52 hours on Eloctate[®]; 5%: 79 hours on Jivi[®] vs 67 hours on Eloctate[®]; 3%: 91 hours on Jivi[®] vs 79 hours on Eloctate[®]; 1%: 117 hours on Jivi[®] vs 104 hours on Eloctate[®].

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References: Anderson PL. The ABCs of pharmacokinetics. <http://www.thebody.com/content/art875.html>. Accessed April 2018. • Collins PW, Blanchette VS, Fischer K, et al. Break-through bleeding in relation to predicted factor VIII levels in patients receiving prophylactic treatment for severe hemophilia A. *J Thromb Haemost*. 2009;7(3):413-420. • Data on file, Tx Review 1018, Bayer; 2018. • Dhillon S, Gill K. Basic pharmacokinetics. In: Dhillon S, Kostrzewski A, eds. *Clinical Pharmacokinetics*. London, UK: Pharmaceutical Press; 2006. • Jivi[®] Prescribing Information. Whippany, NJ: Bayer LLC; 2018. • Merriam-Webster Medical Dictionary. www.merriam-webster.com/medical. Accessed June 2019. • 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 Inc; 2003. • 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;1-10. <https://link.springer.com/article/10.1007%2Fs00277-019-03747-2>. Published June 24, 2019. Accessed June 25, 2019.

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Jivi[®]
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