# Policy Type: PA/SP  Pharmacy Coverage Policy: EOCCO029

**Description**

Adynovate, Eloctate, and Jivi are extended half-life factor VIII products for the treatment and prevention of bleeding in patients with hemophilia A.

**Length of Authorization**

- Initial: 6 months (for on-demand and prophylaxis); 1 month (for perioperative)
- Renewal: 12 months (for prophylaxis); 6 months (for on-demand)

**Quantity limits**

| Product Name | Dosage Form | Indication/ FDA Labeled Dosing | Quantity Limit‡ |
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| **Adynovate**, antihemophilic factor (recombinant), PEGylated | 250, 500, 750, 1000, 1500, 2000, 3000 IU | **On-demand Treatment:** Up to 50 IU/kg every 8 to 24 hours until bleeding is resolved<br><br>**Routine Prophylaxis:**<br>• ≥12 years: Up to 50 IU/kg two times per week<br>• <12 years: 55 IU/kg two times per week with a maximum of 70 IU/kg<br><br>**Perioperative Management:**<br>• *Minor* (e.g. tooth extraction): Up to 50 IU/kg within one hour before surgery; Repeat after 24 hours as needed until bleeding is resolved<br>• *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 60 IU/kg within one hour before operation; Repeat every 8-24 hours (6 to 24 hours for patients <12 years of age) until adequate round healing | **On-demand Treatment:** Up to the number of doses requested every 28 days<br><br>**Routine Prophylaxis:**<br>• ≥12 years: Up to 420 IU/kg every 28 days<br>• <12 years: Up to 590 IU/kg every 28 days<br><br>**Perioperative Management:**<br>Up to the number of doses requested for 28 days |

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| **Eloctate**, antihemophilic factor (recombinant), Fc fusion protein | 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 5000, 6000 IU | **On-demand Treatment:** Up to 50 IU/kg every 12 to 24 hours (every 8 to 24 hours in patients <6 years of age) until bleeding is resolved<br><br>**Routine Prophylaxis:**<br>• ≥6 years: Up to 65 IU/kg every three to five days<br>• <6 years: Up to 65 IU/kg every three to five days. More frequent or higher doses (up to 80 IU/kg) may be required<br><br>**Perioperative Management:**<br>• *Minor* (e.g. tooth extraction): Up to 40 IU/kg every 24 hours (every 12-24 hours for patients <6 years of age) for at least 1 day until healing is achieved<br>• *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Preoperative dose of up to 60 IU/kg followed by a repeat dose of up to 50 IU/kg after 8-24 hours (6-24 for patients <6 years of age) and then every 24 hours until adequate wound healing (at least 7 days) | **On-demand Treatment:** Up to the number of doses requested every 28 days<br><br>**Routine Prophylaxis:**<br>• ≥6 years: Up to 820 IU/kg every 28 days<br>• <6 years: Up to 1,010 IU/kg every 28 days<br><br>**Perioperative Management:**<br>Up to the number of doses requested for 28 days |
| **Jivi**, antihemophilic factor (recombinant), PEGylated | 500, 1000, 2000, 3000 IU | **On-demand Treatment:** Up to 50 IU/kg every 8 to 24 hours until bleeding is resolved<br><br>**Routine Prophylaxis:**<br>• ≥12 years: Up to 40 IU/kg two times per week<br>• <12 years: Not FDA approved | **On-demand Treatment:** Up to the number of doses requested every 28 days<br><br>**Routine Prophylaxis:**<br>• ≥12 years: Up to 340 IU/kg every 28 days<br>• <12 years: Not FDA approved |

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| | | **Perioperative Management:**<br>• *Minor* (e.g. tooth extraction): Up to 30 IU/kg within every 24 hours for at least 1 day until healing as achieved<br>• *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 50 IU/kg every 12-24 hours until adequate wound healing is complete, then continue therapy for at least another 7 days | **Perioperative Management:** Up to the number of doses requested for 28 days |

‡Allows for +5% to account for assay and vial availability

### Initial Evaluation

I. Extended half-life factor VIII products may be considered medically necessary when the following criteria below are met:
   A. Member has a confirmed diagnosis of **hemophilia A (congenital factor VIII deficiency)** and the following are met:
      1. Treatment is prescribed by or in consultation with a hematologist; **AND**
      2. Use of extended half-life factor VIII is planned for one of the following indications:
         i. On-demand treatment and control of bleeding episodes **AND** the number of factor VIII units requested does not exceed those outlined in the Quantity Limits table above for routine prophylaxis; **OR**
         ii. Perioperative management of bleeding; **OR**
         iii. Routine prophylaxis to reduce the frequency of bleeding episodes when one of the following is met:
            a. Member has severe hemophilia A (defined as factor VIII level of <1%); **OR**
            b. Member has had more than one documented episode of spontaneous bleeding; **AND**
      3. Prior treatment with a standard half-life factor VIII product administered at the FDA approved dose for at least 50 exposure days was ineffective for the treatment or prevention of bleeding episodes; **OR**
      4. There is clinical documentation that all available standard half-life factor VIII products are inappropriate; **AND**

5. Documentation that inhibitor testing has been performed within the last 12 months AND if inhibitor titers are high (≥5 Bethesda units), there is a documented plan to address inhibitors; **AND**
6. Dose and frequency does not exceed those outlined in the Quantity Limit Table above, unless documented clinical reasoning for higher dosing and/or frequency is supported by a half-life study to determine the appropriate dose and dosing interval; **AND**
7. If the request is for Jivi, the member is 12 years of age or older and has been previously treated with factor VIII

II. Extended half-life factor VIII products are considered investigational when used for all other conditions.

## Renewal Evaluation

I. For **on-demand treatment** and **routine prophylaxis**:
   i. Documentation of clinical benefit, including decreased incidence of bleeding episodes or stability of bleeding episodes relative to baseline; **AND**
   ii. Documentation that inhibitor testing has been performed within the last 12 months AND if inhibitor titers are high (≥5 Bethesda units), there is documented plan to address inhibitors; **AND**
   iii. *For **on-demand treatment only***, the dose and frequency is not greater than the routine prophylactic dose outlined in the Quantity Limit Table above

## Supporting Evidence

I. Hemophilia A (factor VIII deficiency) is an X-linked inherited coagulation factor deficiency that results in lifelong bleeding disorders. The availability of factor replacement products has dramatically improved care for those with hemophilia A.
II. There are varying severities of hemophilia A depending on the level of factor produced by the patient. Hemophilia A is divided into the following categories based on severity:
   i. **Severe**: <1% factor activity (<0.01 IU/mL)
   ii. **Moderate**: Factor activity level ≥ 1% of normal and ≤ 5% of normal (≥ 0.01 and ≤ 0.05 IU/mL)
   iii. **Mild**: Factor activity level >5% of normal and < 40% of normal (> 0.05 and < 0.40 IU/mL
III. There are three general approaches to bleeding management in those with hemophilia A:
   - Episodic ("on demand") treatment that is given at the time of clinically evident bleeding
   - Perioperative management of bleeding for those undergoing elective surgery/procedures
   - Routine prophylaxis is administered in the absence of bleeding to reduce bleeding and long-term complications of bleeding (e.g. arthropathy)

II. The current standard of care for hemophilia A is to replace the deficient coagulation factor either through episodic ("on demand") treatment given at the time of bleeding, or through continuous prophylaxis to prevent bleeding. Recombinant factor VIII products are the treatment of choice for hemophilia A as recommended by The National Hemophilia Foundation's Medical and Scientific Advisory Council (MASAC).

III. MASAC recommends that prophylaxis be considered optimal therapy for individuals age one and older with severe hemophilia A. Therapy should be initiated early with the goal of keeping the trough factor VIII level above 1% between doses.

IV. For individuals who have had more than one bleeding episode (e.g. two or more bleeds into a target joint, evidence of joint disease by physical exam or radiography), prophylaxis may be appropriate to prevent further morbidity, regardless of factor activity level.

V. The safety and efficacy of the extended half-life products were established based on open-label, non-randomized trails. All are effective for reduction in annualized bleeding rates when used prophylactically compared to on-demand treatment.

VI. Extended half-life factor VIII products were developed to extend the half-life and allow for longer infusion intervals. The majority of published clinical trial evidence evaluating extended half-life products have included previously treated patients with a minimum of 50 exposure days and no history of inhibitors.

VII. There is no evidence that extended half-life factor replacement products are safer or more effective than standard half-life products. There are no head-to-head trials comparing extended half-life products and standard half-life products to definitively establish superior safety or efficacy.

## Investigational or Not Medically Necessary Uses

There is no evidence to support the use of extended half-life factor VIII products in any other condition.

## References

1. Adynovate® [Prescribing Information]. Westlake Village, CA: Shire; May 2018
2. Afstyla® [Prescribing Information]. Kankakee, IL: CSL Behring; September 2017
3. Eloctate® [Prescribing Information]. Waltham, MA: Bioverativ Therapeutics; December 2017
4. Jivi® [Prescribing Information]. Whippany, NJ: Bayer; August 2018
5. National Hemophilia Foundation. Hemophilia A. Available from: https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-A. Accessed July 5, 2019.
6. National Hemophilia Foundation. MASAC Recommendations Concerning products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. Available from: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed July 5, 2019.
7. UpToDate, Inc. Hemophilia A and B: Routine management including prophylaxis. UpToDate [database online]. Last updated February 11, 2019.

**Policy Implementation/Update:**

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| Date Created | August 2019 |
| Date Effective | August 2019 |
| Last Updated | August 2019 |
| Last Reviewed | 08/2019 |

| Action and Summary of Changes | Date |
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| New policy created for extended half-life factor products | 08/2019 |