ADYNOVATE
Rurioctocog alfa pegol
(Recombinant Coagulation
Factor VIII, PEGylated)

DOSING GUIDE

ADYNOVATE, Antihemophilic Factor (Recombinant), PEGylated, is a human antihemophilic factor indicated in children and adults with hemophilia A (congenital factor VIII deficiency) for:

- On-demand treatment and control of bleeding episodes
- Perioperative management
- Routine prophylaxis to reduce the frequency of bleeding episodes

Limitation of Use
ADYNOVATE is not indicated for the treatment of von Willebrand disease.

Takeda

PROPHYLAXIS DOSING:
A FLEXIBLE TREATMENT REGIMEN[1†]

		
Dose (IU/kg)	40–50	55 (Maximum 70)
Dose frequency	Twice-weekly	Twice-weekly

- Dosage and duration of treatment depend on the severity of factor VIII deficiency, the location and extent of the bleeding, and the patient's clinical condition.[1]
- Potency assignment is determined using a one-stage clotting assay. Plasma factor VIII levels can be monitored clinically using a one-stage clotting assay.[1]
- Patients vary in their pharmacokinetic (e.g., clearance, half-life, *in vivo* recovery) and clinical response. Base the dose and frequency of ADYNOVATE on the individual clinical response.[1]

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† Please refer to ADYNOVATE® full prescribing information for complete dosing and administration instructions

ON-DEMAND DOSING:
FOR CONTROL OF BLEEDING EPISODES[1†]

Degree of bleeding	Factor VIII level required (% or IU/dL)	Dose* (IU/kg)	Frequency of dose	Duration of therapy
Minor Early hemarthrosis, mild muscle bleeding, or mild oral bleeding episode	20–40	10-20	Every 12–24 hours	Until bleeding is resolved
Moderate Moderate Muscle bleeding, moderate bleeding into the oral cavity, definite hemarthroses, and known trauma.	30–60	15-30	Every 12–24 hours	Until bleeding is resolved
Major Significant gastrointestinal bleeding, intracranial, intra-abdominal or intrathoracic bleeding, central nervous system bleeding, bleeding in the retropharyngeal or retroperitoneal spaces or iliopsoas sheath, fractures, head trauma.	60–100	30-50	Every 8–24 hours	Until bleeding is resolved

*Dose (IU) = Body Weight (kg) x Desired factor VIII Rise (IU/dL or % of Normal) x 0.5 (IU/kg per IU/dL)[1]

IU: International Units

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PERIOPERATIVE DOSING: FOR SURGICAL PROPHYLAXIS[1†]

Type of Surgery	Factor VIII level required (% or IU/dL)	Dose* (IU/kg)	Frequency of dose	Duration of therapy
Minor including tooth extraction)	30-60	30-50	Within one hour before surgery. Repeat after 24 hours if necessary	Single dose or repeat as needed until bleeding is resolved
Major Intracranial, intra- abdominal, or intrathoracic surgery, joint replacement surgery	80-100 (pre- and post- operative)	40-60	Within one hour before the operation to achieve 100% activity. Repeat every 8 to 24 hours (6 to 24 hours for patients <12 years of age) to maintain FVIII activity within the target range.	Until adequate wound healing

*Dose (IU) = Body Weight (kg) x Desired factor VIII Rise (IU/dL or % of Normal) x 0.5 (IU/kg per IU/dL)[1]

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ADYNOVATE® AVAILABLE IN 250IU AND 500IU*

RECONSTITUTE ADYNOVATE IN THREE SIMPLE STEPS**[1]

Available in **2 ml**

- Easy activation for reconstituting ADYNOVATE® in a BAXJECT III system[1]
- Eliminates the need to disinfect the vial, as vials are already assembled in the system housing[2]
- Store ADYNOVATE® in powder form at 2 - 8 °C[1]
- ADYNOVATE® may be stored at room temperature not to exceed 30°C (86°F) for a period of up to 3 months not to exceed the expiration date[1]

*Adynovate is registered in 250IU, 500IU, 750IU, 1000IU, 1500IU, 2000IU, 3000IU strength. Not all strengths are marketed in Malaysia. Please check with Takeda representative for more information.

**Defined as steps involved in transfer of diluent, swirling to dissolve, withdrawal.1 All other steps defined as minor.

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DOSING:
FREQUENTLY ASKED QUESTIONS[1-4]

Q **Once my patient is on ADYNOVATE®, will I need to adjust their dose?**

A In clinical trials, 98% (118/120) of adults and adolescents (≥12 years old)[3], and 91% (60/66) of children (<12 years old)[4] did not require a dose adjustment on prophylaxis treatment. Two adults required an increased dose to 60 IU/kg due to bleeding in target joints.[1] In children, reported reasons for dose adjustment were factor VIII trough levels <1%, increased risk of bleeding and bleeding episodes.[4]

Q **How can I personalise my patients' ADYNOVATE® dose?**

A Over the course of treatment, appropriate determination of factor VIII levels is advised to guide the dose to be administered and the frequency of repeated infusions. It's important to remember that individual patients may vary in their pharmacokinetic (e.g., clearance, half-life, *in vivo* recovery) and clinical response.[1]

Q **Do I need to monitor patients during the course of their treatment with ADYNOVATE®?**

A As individual patients may vary in their response to factor VIII, monitor plasma factor VIII activity by performing a validated one-stage clotting assay to confirm the adequate factor VIII levels have been achieved and maintained. In the case of major surgery, consideration should be given to maintain a factor VIII activity at or above the target range.[1]

Monitor for the development of factor VIII inhibitors. Perform the Bethesda inhibitor assay to determine if factor VIII inhibitor is present. If expected factor VIII activity plasma levels are not attained, or if bleeding is not controlled with the expected dose of ADYNOVATE, use Bethesda Units (BU) to determine inhibitor levels.[1]

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How should ADYNOVATE® be stored?

Store ADYNOVATE in powder form at 2°C to 8°C (36°F to46°F).

- Do not freeze.
- ADYNOVATE may be stored at room temperature not to exceed 30°C (86°F) for a period of up to 3 months not to exceed the expiration date. If stored at room temperature, write the date on the carton when ADYNOVATE is removed from refrigeration.
- After storage at room temperature, do not return the product to the refrigerator.
- Do not use beyond expiration date printed on the carton or housing.
- Store ADYNOVATE in the original box and protect from extreme exposure to light.[1]

What should I recommend if a patient misses a dose?

Advise your patient to proceed with their next dose immediately and continue at the regular prescribed intervals. Patients must not administer a double dose to make up for a missed dose.[2]

Can my patients overdose when administering ADYNOVATE®?

No symptoms of overdose with recombinant coagulation factor VIII have been reported.[1]

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ADYNOVATE 250IU, 500IU, 750IU, 1000IU, 1500IU, 2000IU, 3000IU (human coagulation factor VIII (rDNA), rurioctocog alfa pegol)
ABBREVIATED PRESCRIBING INFORMATION

Please refer to full package insert before prescribing (6th Oct 2021/ USPI, CCDS version 5.0 & 6.0)
Active Ingredient: 250IU, 500IU, 750IU, 1000IU, 1500IU, 2000IU, 3000IU (human coagulation factor VIII (rDNA), rurioctocog alfa pegol. **Indication:** ADYNOVATE, Antihemophilic Factor (Recombinant), PEGylated, is a human antihemophilic factor indicated in children and adults with hemophilia A (congenital factor VIII deficiency) for: On-demand treatment and control of bleeding episodes, Perioperative management, Routine prophylaxis to reduce the frequency of bleeding episodes. Limitation of Use ADYNOVATE is not indicated for the treatment of von Willebrand disease. **Posology and Administration:** Dosage and duration of treatment depend on the severity of factor VIII deficiency, the location and extent of the bleeding, and the patient's clinical condition. Careful monitoring of replacement therapy is necessary in cases of serious or life-threatening bleeding episodes. Patients vary in their pharmacokinetic (e.g., clearance, half-life, in vivo recovery) and clinical response. Base the dose and frequency of ADYNOVATE on the individual clinical response. Refer to package insert for Dosing for On-demand Treatment and Control of Bleeding Episodes and Dosing for Perioperative Management. Routine Prophylaxis: Administer 40-50 IU per kg body weight twice weekly in adults and adolescents (12 years and older). Administer 55 IU per kg body weight two times per week in children (< 12 years) with a maximum of 70 IU per kg. Adjust the dose and dosing intervals based on the patient's clinical response. The safety and efficacy of ADYNOVATE in previously untreated patients have not yet been established. No data are available. **Contraindications:** ADYNOVATE is contraindicated in patients who have had prior anaphylactic reaction to ADYNOVATE, to the parent molecule (ADVATE), mouse or hamster protein, or excipients of ADYNOVATE (e.g. Tris, mannitol, trehalose, glutathione, and/or polysorbate 80). **Warnings and Precautions:** Hypersensitivity Reactions, Neutralizing Antibodies, Monitoring Laboratory Tests. **Interactions:** No interactions of human coagulation factor VIII (rDNA) products with other medicinal products have been reported. **Fertility, Pregnancy and Lactation:** There are no data with ADYNOVATE use in pregnant women to inform a drug- associated risk. ADYNOVATE should be given to a pregnant woman only if clearly needed. There is no information regarding the presence of ADYNOVATE in human milk, the effect on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ADYNOVATE and any potential adverse effects on the breastfed infant from ADYNOVATE or from the underlying maternal condition. **Undesirable Effects:** The most common adverse reactions (≥1% of subjects) reported in the clinical studies were headache, diarrhea, rash, nausea, dizziness and urticaria. Adverse reactions reported during clinical studies include diarrhea, nausea, ocular hyperaemia, hypersensitivity, headache, dizziness, rash, urticaria, drug eruption, flushing, eosinophil count increased, infusion related reaction. **Storage condition:** Store ADYNOVATE in powder form at 2°C to 8°C (36°F to 46°F). Do not freeze. ADYNOVATE may be stored at room temperature not to exceed 30°C (86°F) for a period of up to 3 months not to exceed the expiration date. **Name and Address of Product Registration Holder:** Takeda Malaysia Sdn Bhd, Unit TB-L13-1, Level 13, Tower B, Plaza 33, No.1 Jalan Kemajuan, Seksyen 13, 46200 Petaling Jaya, Selangor, Malaysia.

Further information is available on request.

Suspected Adverse events should be reported to Takeda at: AE.VMAPS@takeda.com

Date of Preparation of the API: 7th Feb 2022
Document number: pi-01641

For Healthcare Professionals Only

References: 1. Adynovate® Malaysia Prescribing Information 6th Oct 2021 2. ADYNOVATE Consumer Medicine Information, March 2022.
3. Konkle BA *et al. Blood* 2015;126:1078–85. 4. Mullins *et al. Haemophilia* 2017;23:238–46.

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C-APROM/MY/ADY/0029 SEPT2022

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