ALBERTA PRECISION LABORATORIES
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ADYNOVATE®
Anti-hemophilic Factor (Recombinant)

APPLICABILITY: This document applies to APL, AHS, Covenant Health, and all other health care professionals involved in the transfusion of blood components and products in Alberta.	***Other Names:*** recombinant Factor VIII, Antihemophilic factor ***Company:*** *Takeda Pharmaceutical Company* ***Class:*** *Manufactured recombinant factor, extended half-life*

	INTRAVENOUS			OTHER		
ROUTES	**DIRECT IV**	**IV Infusion**	**Continuous Infusion**	**SC**	**IM**	**OTHER**
Acceptable Routes*	Yes**	No	No	No	No	N/A

* Administration of blood components and blood products is a restricted activity. For specific conditions that apply to a profession's authorization to administer blood components and blood products, consult the applicable discipline-specific regulation under the Health Professions Act (Alberta). Health care professionals with this authorization require the applicable education, training and competency.
** Direct IV administration of blood products may be performed by health care professionals that have authorization of administration of blood products within their scope of practice.

DESCRIPTION:

- Adynovate® is a sterile, non-pyrogenic, lyophilized, PEGylated recombinant human coagulation factor VIII.
- Product is white to off-white lyophilized powder.
- Reconstituted solution is clear and colourless.
- Available in dose sizes of 250, 500, 1000, 1500, 2000, and 3000 IU.
- Vials are reconstituted with 2mL or 5mL sterile water for Injection.
- Each Adynovate® vial contains the labeled amount of Factor VIII potency expressed in IU per vial.
- Also contains histidine, sodium chloride, calcium chloride, mannitol, glutathione, trehalose dehydrate, tris(hydroxymethyl)-aminomethan and Polysorbate 80.
- Preservative-free.
- Latex-free.

AVAILABILITY:

- Supplied by Canadian Blood Services.
- Contact your local laboratory/transfusion service regarding stock availability on site.

INDICATIONS:

- For adults and children with hemophilia A (congenital Factor VIII Deficiency) for:
  - Routine prophylaxis to reduce the frequency of bleeding episodes.
  - Control and prevention of bleeding episodes.
  - Perioperative management (surgical prophylaxis).

CONTRAINDICATIONS:

- Patients with known hypersensitive to the product or any ingredient in the formulation or component of the container, including hamster proteins, and the parent molecule Advate®.
- Patients with von Willebrand disease (does not contain von Willebrand Factor).

WARNINGS:

- The formation of neutralizing antibodies (inhibitors) is a known complication in the management of individuals with Hemophilia A. All patients treated with coagulation FVIII should be carefully monitored for the development of inhibitors by appropriate clinical observations and laboratory tests.
- The product contains traces of hamster proteins, which in some patients may cause allergic reactions.
- Anaphylaxis and anaphylactoid reactions are possible.
- PEG exposure levels resulting from Adynovate® therapy are very low. Based upon available experimental data, there is also a lack of evidence supporting the potential for accumulation of the specific PEG (20kDA) used in the PEGylation of Adynovate®. The potential for PEG accumulation with Adynovate® is therefore considered to be low.

DOSE (Refer to Product Insert):

- Dose to be determined by the most responsible health practitioner (MRHP) only after consult with Hematologist or bleeding disorders clinic.
- Refer to patient's care plan or Factor First card, if available.
- Dosage and duration of treatment depend on the severity of the factor VIII deficiency, the location and extent of bleeding, presence of inhibitors, Factor VIII level desired, and the patient's clinical condition and individual clinical response.
- Administer up to 80 IU per kg to maintain targeted factor VIII trough levels greater than or equal to 1%. Adjust the dose and/or dose frequency based on the patient's clinical response.
- The calculation of the required dose of FVIII is based on the empirical finding that 1 IU FVIII per kg body weight raises the plasma FVIII activity by 2 IU/dL.

Manufacturer Recommended Dosing:

Indication	Situation	Target (% of normal FVIII)	Recommended Dosing
Prophylaxis	Pediatric (under 12 years)	N/A	40-60 IU/kg two times weekly.
	Adults and adolescents (12 years and over)	N/A	40-50 IU/kg two times weekly.
On-demand	Minor Bleeding:	20-40	10-20 IU/kg Repeat every 12-24 hours until bleeding resolves.
	Moderate Bleeding	30-60	15-30 IU/kg Repeat every 12-24 until bleeding resolves.
	Major Bleeding	60-100	30-50 IU/kg Repeat every 8 to 24 hours until bleeding resolves.
Perioperative management	Minor Surgery:	60-100	30-50 IU/kg single dose within one hour before surgery. Repeat every 8-24 hours to maintain factor VIII trough levels at 30-60% of normal for the first postoperative 24 hours or longer.
	Major Surgery:	80-120 (pre- and post-operative)	40-60 IU/kg single dose within one hour before the operation. **Day 1 to 3 (first 72 hours):** Repeat Dose every 8-24 hours to maintain factor VIII trough levels of at least 80%. **Day 4 to 7:** Repeat doses every 8-24 hours to maintain factor VIII trough levels of at least 50%. **After day 7**: Repeat doses every 8-24 hours to maintain factor VIII trough levels of at least 30%.
*Dosage Required (IU) = Body Weight (kg) × Desired Factor VIII Increase (IU/dL or % normal) × 0.5 (IU/kg per IU/dL)			

ADMINISTRATION:

Confirm written (signed) consent has been obtained and documented prior to requesting blood component from lab/transfusion service where possible.

Pre-Infusion:

- Ensure recent patient weight and height is on file.
- Ensure pertinent labs are available as required (ie. Factor VIII)
- Ensure any ordered premedications have been given (antihistamines, antipyretics prn).
- Perform pre-transfusion checks per AHS Transfusion of Blood Components and Blood Products Policy.
- Report any new onset acute illness to the authorized prescriber prior to commencing infusion.

Access: Adynovate® can be given via peripheral or central venous access site.

Reconstitution Supplies:

- Adynovate® Product (lyophilized powder).
- Sterile water for injection (included with product).
- BAXJECT II High-Flow reconstitution device (included with product)
- Antiseptic swabs (not included with product)
- Sterile plastic Luer lock syringe, large enough to contain dose (provided separately with product)

Reconstitution:

- Bring the product and diluent to room temperature prior to reconstitution.
- Refer to Baxject II Reconstitution Instructions.
- Adynovate® should be visually inspected for particulate matter and discoloration prior to administration. Do not use solutions that are visibly cloudy or have deposits.

Compatible IV Solutions:

- Do not mix with other medicinal products or solutions.
- Normal saline can be used to flush the line.

Administration Supplies:

- Antiseptic swabs
- Infusion set (provided separately with product)

Administration:

- Adynovate® should be administered immediately and no later than 3 hours after reconstitution.
- If product cannot be administered immediately, refer to storage and stability section below.
- **Administration rate:**
  - Administration rate should be specified by the MRHP after patient assessment.
  - Administer over a period of up to 5 minutes (maximum infusion rate 10mL per in), as determined by patient comfort, or as requested by MRHP or bleeding disorder clinic.

POTENTIAL HAZARDS WITH PARENTERAL ADMINISTRATION:

- Potential adverse events related to a blood product transfusion range in severity from minor with no sequelae to life-threatening.
- All adverse events occurring during a transfusion should be evaluated to determine whether or not the transfusion can be safely continued/restarted.
- All adverse events suspected to be related to a product transfusion (whether during or after a transfusion) must be reported to your local transfusion service.
- Allergic-type hypersensitivity reactions including anaphylaxis have been reported and have manifested as pruritis, rash, urticaria, hives, facial swelling, dizziness, hypotension, nausea, chest discomfort, cough, dyspnea, wheezing, flushing, discomfort (generalized) and fatigue.
- The most commonly reported adverse reactions in patients receiving Adynovate® are headache, diarrhea, dizziness, nausea, and rash.

Side Effects - Flushing - Headache - Nausea - Itching / redness at infusion site	→	**Action:** Slow rate of infusion
Potential Allergic Reaction - Difficulty breathing or swallowing - Chest tightness - Hives/severe itching - Swelling of lips and tongue - Dizziness - Pale and cold skin - Fast heartbeat - Red or swollen face or hands	→	**Action:** **STOP** infusion **IMMEDIATELY** and contact physician

NURSING IMPLICATIONS:

Patient Monitoring:

- Vital Signs: Pre-administration**,** on completion of dose, and as patient condition requires.
- If the patient has experienced previous adverse reaction to product transfusion, or this is the first transfusion of product for patient, monitor for 30-60 minutes post.

Patients receiving blood product transfusions must be observed closely for signs of any unexpected or untoward reactions. These reactions may occur during or after the infusion of blood or blood products. For follow up instructions to a transfusion reaction, go to: http://www.albertahealthservices.ca/lab/page4240.aspx

Documentation:

- Ensure documentation is completed per the AHS Transfusion of Blood Components and Blood Products Policy.
- Patient tolerability should be documented in appropriate flow chart or clinical record (electronic or paper).
- Document vital signs as required in the appropriate flow chart or clinical record (electronic or paper).
- Provide patient notification documentation where required.

STORAGE & STABILITY:

- The lyophilized powder may be stored at refrigerated temperatures of 2°C to 8°C until expiration date on box.
- The lyophilized powder may also be stored at room temperate (not to exceed 30°C) for up to 3 months. Once stored above refrigerated temperature, do not return the product to refrigerated storage.
- The reconstituted Adynovate® must be used within 3 hours after reconstitution.
- Protect from light.
- Do not freeze.

CONTACT INFORMATION:

Approved By: APL Transfusion Medicine Discipline Council
For questions or comments please contact Transfusion.SafetyTeam@aplabs.ca

REFERENCES

Takeda Canada Inc. 24 February 2022. Adynovate® Product Monograph. Submission Control No 259343. [Accessed 10Jun22]. https://www.takeda.com/4aba60/siteassets/en-ca/home/what-we-do/our-medicines/product-monographs/adynovate/adynovate-pm-en.pdf