Class: Manufactured blood product (human) - anticoagulant	Alternate Product Name: • Antithrombin • AT III	Company/Supplier: • Takeda

Routes	Intravenous			Other		
	Direct IV	IV Infusion	Continuous Infusion	SC	IM	Other
Acceptable routes*	Yes	Yes * see administration	No	No	No	N/A

Description	• Antithrombin III (AT III) acts as a physiological inhibitor of blood coagulation, particularly by inhibition of thrombin and activated Factor 10 (X), but also Factors 9a (IXa), 10a (Xa) 11a (XIa), 12a (XIIa) and plasmin. • The inhibitory effect of AT III is accelerated within the presence of heparin. • AT III is supplied as a freeze-dried powder with diluent for intravenous administration.
Availability	• **Vial sizes/dosages:** • 1000 units (900-1100 units/vial, supplied with 20 mL Sterile Water for Injection) • Supplied by Canadian Blood Services (CBS). • **Contact <u>your</u> local laboratory/transfusion laboratory service regarding in house stock availability at your site.**
Indications	• Prophylaxis and treatment of thrombotic and thromboembolic disorders in patients with hereditary AT III deficiency (activity below 70% of normal). • May be used for management of Heparin Resistance due to acquired AT III deficiency in patients requiring unfractionated heparin products for anticoagulation who are unable to achieve therapeutic levels despite large doses (e.g. patients on extracorporeal life support with subtherapeutic aPTT or anti-Xa levels, or in the setting of cardiopulmonary bypass with Activated Clotting Time (ACT) less than 480 seconds following bolus heparin dosing) – *off label.*
Contraindications	• Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. • Known history of heparin-induced thrombocytopenia. • For a complete listing, see the Contraindications section of product monograph. <u>https://www.takeda.com/49a55e/siteassets/en-ca/home/what-we-do/our-medicines/product-monographs/antithrombin-iii/antithrombin-iii-nf-pm-en.pdf</u>
Warnings	• Product half-life may be significantly reduced with concomitant heparin treatment due to accelerated antithrombin turnover and in cases of disseminated intravascular coagulation. • Products made from human plasma may contain infectious agents, such as viruses and, theoretically, the variant Creutzfeldt-Jakob disease (vCJD) agent that can cause disease.

	The risk that such products will transmit an infectious agent has been reduced by plasma donor screening, testing for the presence of certain current viruses, and by viral inactivation/removal steps. There is also the possibility that unknown infectious agents may be present in such products. • The anticoagulant effect of heparin is enhanced by concurrent administration of AT III leading to increased risk of hemorrhage. Dose adjustment of unfractionated heparin based on aPTT or anti-Xa levels must be performed at close intervals in the first few hours after initiation of AT III and regularly afterwards. • Patients with a bleeding diathesis should be monitored closely for hemorrhagic complications when receiving heparin and AT III in conjunction.
Dosage	• **Dosage should be determined by a physician experienced in the care of patients with AT III deficiency.** • Individual dosing may vary based on the based-on body weight, laboratory values, and the cause and severity of AT III deficiency; a decrease in activity below 70% of normal is associated with an increased risk of thrombosis. • When the indication for antithrombin substitution is established, the dosage should be sufficient to reach the target antithrombin activity (80-120%), and to maintain an effective level. • For further information about dosage please review the product monograph. • **Consult with the Transfusion Medicine Physician on-call for safe dosing recommendations, available through switchboard at (306) 655-1000.**
Pre-administration Testing Requirements	• Test the plasma AT III level to confirm the presence of congenital or acquired AT III deficiency prior to administering this product. The patient clinical condition must be considered. • In the setting of Cardiopulmonary Bypass, ACT level alone may guide AT III product request. Note: Draw of a pre-administration AT III plasma level (reported after the product is given) is strongly recommended to help guide additional product dosing, as appropriate.
Ordering	• Specify type of coagulation concentrate and dosage required. • To request product from the transfusion medicine laboratory, use the “Plasma Protein Product Request Form” #103221.
Forms Required	• Informed Consent for Blood Components and/or Plasma Protein Products #101479. • Plasma Protein Product Request Form #103221. • Transfusion/Infusion Administration and Assessment Record #101059. • Saskatchewan Transfusion Adverse Event Report Form #103695 (only needed if adverse event occurs). • Notification of Administration of Blood and/or Blood Products Form #103854. • **Forms can be located in the Lab Services Manual or Forms on Demand** **https://www.saskatoonhealthregion.ca/locations_services/Services/Pathology-Laboratory-Med/healthpractitioners/Pages/requisitions.aspx**

Supplies required	• The product package contains:
	  • one single-use Antithrombin III vial.
	  • one single-use sterile water for Injection vial (20 mL for diluent).
	  • a sterile double-ended needle.
	  • a sterile filter needle.
	• Additional supplies needed:
	  • one luer lock syringe (appropriate size based on volume) for administration.
	  • alcohol swab (for cleaning the tops of the vials).

Administration	• **Blood consent:** Is required due to human plasma component. • **Pre-infusion:** Ensure recent patient weight is on file and pertinent laboratory results are available. • Perform all other appropriate pre-transfusion checks per protocol. See "Policies and Procedures of Blood Components and Plasma Protein Products - Administration of #1141." • **Administration:** ***Administered at room temperature by slow intravenous injection at a rate not exceeding 5 mL per minute (20 mL in 4 minutes).*** • For additional preparation/reconstitution and administration steps see Administration section of the Product Monograph • **Access:** can be given via CVC, PICC, or peripheral IV. • **Compatible Solutions:** Can flush line with 0.9% normal saline pre and post administration of AT III. No other drugs / solutions (including normal saline) can be co-administered in the same line while AT III is being infused. • **Reconstitution:** NOTE: Reconstitute immediately before administration. Administer within minutes after reconstitution. Entered vials must not be reused. The product does not contain a preservative and must be handled with aseptic technique to prevent contamination. DO NOT refrigerate after reconstitution. DO NOT further dilute in any IV solutions. DO NOT mix with other drugs or IV solutions

Use aseptic technique (clean and germ free) when preparing and reconstituting Antithrombin III NF®

1. Warm the unopened bottle containing Sterile Water for Injection (diluent) to room temperature	
2. Remove protective caps from the rubber-capped vials containing the powder and the solvent (fig. A) and cleanse the rubber stoppers of both.	 fig.A
3. Remove protective covering from one end of the enclosed transfer needle by twisting and pulling. Insert the needle through the rubber stopper of the solvent vial (fig. B and C).	 fig.B fig.C
4. Remove protective covering from the other end of the transfer needle taking care not to touch the exposed end.	
5. Invert the solvent vial over the powder vial and insert the free end of the transfer needle through the rubber stopper of the powder vial (fig. D). The solvent will be drawn in by the vacuum in the powder vial.	 fig.D
6. After the entire solvent has flowed into the powder vial, disconnect the two vials by removing the transfer needle from the powder vial (fig. E). Gently agitate the powder vial to accelerate dissolution.	 fig.E
7. Upon complete reconstitution of the powder, insert the enclosed aeration needle (fig. F) and any foam will collapse. Remove the aeration needle.	 fig.F

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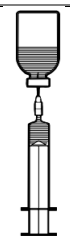
<tr><td>8. Remove protective covering from the enclosed filter needle by twisting and pulling and fit the needle onto the sterile disposable syringe. Draw the solution into the syringe (fig. G).</td><td> 
fig.G</td></tr>
<tr><td>9. Clean the intended injection site with an alcohol swab and attach the luer lock syringe containing AT III. Administer product.</td><td></td></tr>
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Syringe labels with patient identifiers are not required if this product is administered intravenously over less than or equal to 5 minutes.

• Lab testing post administration: AT III level at 60 minutes following product administration to ensure target is reached, and subsequently as directed by the most responsible healthcare provider (MRHP).</td></tr>
<tr><td>Nursing Implications</td><td>• Patient monitoring: Follow the “Nursing Policy and Procedure Blood Components and Plasma Protein Product – Administration of #1141”.
• Documentation: Administration and vital signs shall be recorded on the “Transfusion/Infusion Administration and Assessment Record” #101059.</td></tr>
<tr><td>Adverse Events</td><td>• Allergic reactions are possible with administration of blood components and plasma protein products ranging from mild to life threatening.
• Refer to Nursing Policy and Procedure Blood Components and Plasma Protein Product – Administration of #1141 for managing of allergic transfusion reaction and call MRHP.
• Document adverse event on Saskatchewan Transfusion Adverse Event Report Form #103695, whether or not the transfusion was discontinued.</td></tr>
<tr><td>Comments/References</td><td>• Antithrombin III Product Monograph, revision date April 30, 2021. https://www.takeda.com/49a55e/siteassets/en-ca/home/what-we-do/our-medicines/product-monographs/antithrombin-iii/antithrombin-iii-nf-pm-en.pdfAccessed on August 10, 2021.
• Saskatoon Health Region Policies and Procedures Nursing Policy and Procedure Blood Components and Plasma Protein Product – Administration of #1141 https://www.saskatoonhealthregion.ca/about/NursingManual/1141.pdf Accessed August 10, 2021.
• Saskatoon Clinical Perfusion – Guideline Number 3012. Antithrombin for Heparin Resistance in Cardiopulmonary Bypass. Approval date January 15, 2021.</td></tr>
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