Diphtheria Antitoxin (equine) Biological Page

Section 7:	**Biological Product Information**		**Standard #: 07.202**
Created by:	Provincial Immunization Program		
Approved by:	Provincial Immunization Program		
Approval Date:	July 18, 2014	**Revised:**	June 30, 2023

	Diphtheria Antitoxin Butantan Institute, Brazil	Diphtheria Antitoxin VINS Bioproducts Limited, India
Manufacturer	Butantan Institute, Brazil	VINS Bioproducts Limited, India
Biological Classification	Antitoxin	
Authorization and Access	**Special authorization and access procedures must be followed.** • The Office of the Chief Medical Officer of Health (OCMOH) must be notified by the fastest means possible of all cases in which diphtheria antitoxin is required. • Available on a 24-hour basis from Alberta Health by calling OCMOH pager: 780-638-3630. A Special Access Program (SAP) form is included with the product and must be completed and returned to Alberta Health. Note: Diphtheria Antitoxin (equine) is stocked in the Provincial Vaccine Depot and the Alberta Health Services (AHS) Calgary Vaccine Depot. Both products are currently supplied in Alberta, each with different dosing and scheduling recommendations. Providers will receive the product that is readily available in their zone and will need to refer to the corresponding dosing and scheduling recommendations below.	

Indications for use of diphtheria antitoxin serum	Treatment of suspected (based on clinical symptoms) or confirmed disease. Bacteriologic confirmation is not required to initiate treatment.
	• Eligibility will be determined though discussion amongst the treating physician, the zone Medical Officer of Health (MOH) and Alberta Health Chief Medical Officer of Health
	  ○ Once eligibility has been determined, OCMOH will authorize release of the product through either the Provincial Vaccine Depot or the AHS Calgary Vaccine Depot. It is not routinely stocked outside of these two sites.
	• Special authorization, access and transport procedures must be followed. This includes:
	  ○ Ensuring the biological is packed and transported under strict cold chain management guidelines from the Vaccine Depot to the facility.
	  ○ Obtaining a signature for receipt of product from the treating physician
	  ○ Completion of Special Access Program Form C by the treating physician in conjunction with the zone MOH (a Special Access Program form is included with the product or can be found at http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/sapf3_pasf3-eng.php)
	  ○ Returning the completed Special Access Program Form C to the MOH/MOH designate
	The zone MOH/MOH designate will review the Special Access Program Form C to ensure all fields are completed and then submit the completed form to Alberta Health.
	
	Notes:
	• Not recommended for prophylaxis of close, immunized or unimmunized contacts of diphtheria cases.
	• For further information about the disease and reporting requirements refer to the Public Health Notifiable Disease Management Guidelines – Diphtheria.	

<table>
<tr><th></th><th>Diphtheria Antitoxin Butantan Institute, Brazil</th><th>Diphtheria Antitoxin VINS Bioproducts Limited, India</th></tr>
<tr><td rowspan="3">Schedule</td><td colspan="2">Diphtheria antitoxin serum should be administered as soon as possible after clinical diagnosis. Treatment should not await laboratory confirmation of toxigenic C. diphtheriae.</td></tr>
<tr><td>○ Skin testing for serum hypersensitivity is recommended before administration of diphtheria antitoxin
○ Note: This recommendation differs from the Product Leaflet.
○ For hypersensitivity and desensitization procedures only, refer to US CDC Use of DAT for Suspected Diphtheria Cases - Protocol, specifically sections 6.3 & 6.4, including Tables 3 & 4</td><td>○ Skin testing for serum hypersensitivity is recommended before administration of diphtheria antitoxin
○ See the Product Leaflet for details.</td></tr>
<tr><td colspan="2">See also the product information and Appendix 1 and 2 of Public Health Notifiable Disease Management Guidelines – Diphtheria.
Note: Individuals who have recovered from diphtheria should receive the age-appropriate diphtheria-containing vaccine. The vaccine should be administered three to four weeks after diphtheria antitoxin was administered to minimize antigen-antibody antagonism. Diphtheria infection does not necessarily confer immunity.</td></tr>
<tr><td>Preferred Use</td><td colspan="2">N/A</td></tr>
<tr><td rowspan="2">Dose</td><td colspan="2">The therapeutic dose is determined by the severity of the disease.
Follow the dosage as outlined on the Product Leaflet.
This is a treatment product administered under the direction of a physician in an acute care setting.</td></tr>
<tr><td>Note: Diphtheria antitoxin is supplied in 10 mL vials containing 10,000 IU each. For example, the Product Leaflet recommends 40,000 IU for mild cases and up to a maximum of 100,000 IU for severe cases.</td><td>Note: Diphtheria antitoxin is supplied in 10 mL vials containing 10,000 IU each. For example, the Product Leaflet recommends 10,000 to30,000 IU for mild to moderately severe cases and up to a maximum of 100,000 IU for severe cases.</td></tr>
<tr><td>Route</td><td colspan="2">Refer to the Product Leaflet (enclosed with antitoxin).</td></tr>
<tr><td>Contraindications/ Precautions</td><td colspan="2">Contraindications:
• None as this is a vital indication due to life-threatening condition.
Precautions:
• History of severe hypersensitivity reaction to this antitoxin. Use desensitization protocol if hypersensitivity exists and antitoxin urgently needed. If diphtheria is present, antitoxin must be given.
• Patients should be assessed and tested for hypersensitivity to equine sera prior to administration of diphtheria antitoxin as it may trigger allergic reactions of varying degrees. Refer to product leaflet accompanying the product.</td></tr>
<tr><td>Possible Reactions</td><td colspan="2">Common:
• Serum sickness (fever, itching, urticaria, arthralgia, myalgia, adenomegaly) may occur between 5-24 days following administration
• Allergic reactions of varying severity (including skin pruritus, flushing, angioedema, morbilliform rash, tachycardia, rhinorrhea, sneezing, abdominal cramps, diarrhea, pain, swelling or redness, urticaria, cough, hoarseness, nausea, vomiting and asthma-like crisis). More common in those previously treated with antitoxin of equine origin
Uncommon:
• Chills, sweating</td></tr>
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	Diphtheria Antitoxin Butantan Institute, Brazil	Diphtheria Antitoxin VINS Bioproducts Limited, India
	Rare: • Anaphylaxis • Neurological or renal compromise • Vasculitis • As with any immunization, unexpected or unusual side effects can occur. Refer to the Product Leaflet for more detailed information.	
Pregnancy	• Pregnancy is not a contraindication to the use of diphtheria antitoxin serum. • Intact IgG crosses the placenta from maternal circulation increasingly after 30 weeks.	
Lactation	• Breastfeeding is not a contraindication to diphtheria antitoxin serum. • It is not known if antitoxin antibodies are excreted into breast milk	
Composition	Each 1 mL contains: ○ $F(ab')_2$ equine-derived immunoglobulin fractions ○ phenol ○ saline solution	Each 1 mL contains: ○ enzyme refined, equine Diphtheria antitoxic immunoglobulin fragments, not less than 1000 IU ○ cresol I.P/B.P (preservative): not more than 0.25% v/v ○ sodium chloride I.P/B.P ○ glycine I.P/B.P
Blood/Blood Products	Equine horse serum	
Bovine/Porcine Products	None listed in the ingredient list	
Latex	None listed in the ingredient list	
Interchangeability	N/A	
Administration with Other Products	• Delay administration of products containing diphtheria toxoid for 3 to 4 weeks after diphtheria antitoxin administration to minimize the possibility of antigen-antibody antagonism.	
Appearance	Clear transparent solution	
Storage	• Store at +2ºC to +8ºC. • Once the vial is opened, the preparation should be used immediately. • Do not freeze. • Do not use beyond the labeled expiry date. • Store in the original packaging to protect from light. • If after receiving the product, a clinician determines that it is not required, the unused product must be shipped back to the Provincial Vaccine Depot, preferably under cold chain with at least twice daily documented storage temperatures. See the shipment package for further details.	
Vaccine Code	DA	
Antigen Code	DA	
Licensed for	Currently there is no licensed product made in Canada, and product is made available from Health Canada's Special Access Program (SAP).	

Related Resources:

- AHS-Imm-07.202-R01 (June 1, 2023) Diphtheria Antitoxin (Equine) Information Sheet

References:

1. Alberta Health. Alberta Immunization Policy (2023, June 30). *Diphtheria Antitoxin (equine).*

Alberta Health. Communicable Disease Control and Prevention. (2021, September). Public Health Notifiable Disease Management Guidelines – Diphtheria. In Public health notifiable disease management guidelines. *Public Health Notifiable Disease Management Guidelines – Diphtheria.*

2. American Academy of Pediatrics. (2021). *Red Book: 2021-2024 Report of the Committee on Infectious Diseases* (32nd ed.). Itasca, IL: Author. Butantan Institute. (2019) Diphtheria Antitoxin (DAT). *Product Leaflet*.

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3. Centre for Disease Control and Prevention Protocol. (2022, June 9). *Expanded Access Investigational New Drug (IND) Application Protocol: Use of Diphtheria Antitoxin (DAT) for Possible Diphtheria Cases.* https://www.cdc.gov/diphtheria/downloads/protocol.pdf
4. Grabenstein, J. D. (2012). *ImmunoFacts: Vaccines and Immunologic Drugs - 2013*. St. Louis, MO: Wolters Kluwer Health.
5. VINS BIOPRODUCTS Limited. Diphtheria antitoxin (equine). Product Leaflet.
6. National Advisory Committee on Immunization. (2023). *Canadian immunization guide* (Evergreen edition.). Ottawa, ON: Public Health Agency of Canada. http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-dip-eng.php