

# INSTRUCTIONS FOR RECEIVING BAT<sup>®</sup> ANTITOXIN

Alaska Division of Public Health, Section of Epidemiology (SOE)

Vaccine Depot - 3601 C Street, Suite 586, Anchorage, AK 99503

**Important Notice: Please store enclosed BAT<sup>®</sup> in a monitored FREEZER at or below  $\leq 5^{\circ}\text{F}$  ( $\leq -15^{\circ}\text{C}$ ) until used.**

**Do not re-freeze BAT<sup>®</sup> once it has thawed!**

- Upon receiving immediately check the TempTale Temperature Monitor display. If the TempTale display indicates that a shipping temperature deviation occurred, contact SOE immediately at the number below.
- Visually inspect vial(s). The contents should be completely **FROZEN**.
- If vial is completely frozen and the TempTale display confirmed no temperature deviation during shipment, place the kit in an alarmed monitored **FREEZER  $\leq -15^{\circ}\text{C}$** . If vial is partially or completely thawed, place the kit in an alarmed monitored **refrigerator  $2-8^{\circ}\text{C}$  ( $36-46^{\circ}\text{F}$ )** and contact SOE ASAP.

Return the TempTale Monitor and shipping container to the SOE Vaccine Depot ASAP using a priority, tracked shipping method.

- For problems or other questions call 907-334-0856 or 907-269-8029.**

## CONFIRMATION OF RECEIPT OF BAT<sup>®</sup>:

Date/Time BAT<sup>®</sup> Received: \_\_\_\_\_ Time: \_\_\_\_\_

Kit Number Received: \_\_\_\_\_ Lot No: \_\_\_\_\_ Exp Date: \_\_\_\_\_

Kit Number Received: \_\_\_\_\_ Lot No: \_\_\_\_\_ Exp Date: \_\_\_\_\_

Received Frozen  Yes  No (if No, call the above number)

BAT<sup>®</sup> Received and Visually Inspected by: \_\_\_\_\_

Facility Name: \_\_\_\_\_ Phone: \_\_\_\_\_

**Fax completed confirmation sheet to 907-269-0472 or Scan to DPH-Pharmacist**

## BAT<sup>®</sup> (Botulinum Antitoxin) Kit CHECKLIST

<b>PHARMACY STAFF: UPON RECEIPT OF KIT/PRIOR TO USE</b>	<b>DATE COMPLETED</b>
1. Fill out the bottom portion of the coversheet, titled “Instructions for Receiving BAT <sup>®</sup> Antitoxin”. Fax this back to the Section of Epidemiology Depot at 341-2249.	
2. Store the BAT <sup>®</sup> in the freezer; monitor freezer temperatures. <b>Store frozen at or below ≤ 5°F (≤ -15°C) until used.</b>	
<b>CLINICIANS: IMMEDIATELY UPON USE</b>	<b>DATE COMPLETED</b>
1. <b>If botulism is suspected, call Epidemiology immediately: 907-269-8000 business hours OR 800-478-0084 after-hours.</b>	
2. Provide patients or their guardians with the Patient Information Guide.	
3. Prepare for BAT <sup>®</sup> administration; using the guidance in the package insert (summarized in the Treatment Instructions). If product is frozen, thaw using the guidance in the package insert (summarized in the Treatment Instructions).	
4. Administer BAT <sup>®</sup> .	
5. Report any adverse reactions to Cangene or the FDA as described in the Treatment Instructions.	
<b>HOSPITAL STAFF: WITHIN 48 HOURS OF USE</b>	<b>DATE COMPLETED</b>
1. Notify the Section of Epidemiology Drug Room of the Kit # used and order replacement stock. Phone: 907-334-0856 or 269-8029.	
2. Complete the Case Report form.	
3. Fax completed forms to the Section of Epidemiology at 563-7868.	
<b>HOSPITAL STAFF: UPON PATIENT DISCHARGE OR DEATH</b>	<b>DATE COMPLETED</b>
1. Complete the Clinical Outcome Report form.	
2. Fax completed forms to the Section of Epidemiology at 563-7868.	

**Report all suspected cases of botulism immediately to:**  
**Section of Epidemiology**  
**907-269-8000 during business hours OR 1-800-478-0084 after hours**  
**Epidemiology main fax: 563-7868**  
**Depot fax: 269-0472**

*NOTE: Report Forms from Part B of the Antitoxin Packet are available online at*  
<http://dhss.alaska.gov/dph/Epi/id/Pages/botulism/resources.aspx>

# **BAT<sup>®</sup> (Botulinum Antitoxin) Kit Packing List Overview**

## **PART A – PROVIDER RESOURCES**

- New Treatment Instructions for BAT<sup>®</sup> (Botulinum Antitoxin)
- Package Insert (Revised March 2017)
- Patient Information Guide (last two pages of the package insert)

## **PART B – FORMS**

- Botulism Case Report Form
- Clinical Outcome Report Form to be completed by clinician administering BAT<sup>®</sup> and to be accompanied by a copy of the discharge summary

## **PART C – PRODUCT**

One vial of BAT<sup>®</sup> (Botulinum Antitoxin) product

**Report all suspected cases of botulism immediately to:  
Section of Epidemiology  
907-269-8000 during business hours  
1-800-478-0084 after hours**

# BAT<sup>®</sup> (Botulinum Antitoxin) Kit

## PART A – PROVIDER RESOURCES

- I. New Treatment Instructions for BAT<sup>®</sup> (Botulinum Antitoxin)
- II. Package Insert (Revised March 2017)
- III. Patient Information Guide (last two pages of the package insert)
- IV. General Guidance on Repeat Dosing with BAT<sup>®</sup>
  - **The data for administration of a second dose of BAT<sup>®</sup> during a single episode of botulism is limited. Typically a second dose or vial is not recommended as one vial of BAT<sup>®</sup> contains enough antitoxin to cover all “naturally” occurring foodborne botulism. Other exposures, such as with an intentional release, could have higher toxin loads; special treatment guidance will be given in those situations.**
  - **Clinical situations that may require an additional dose of BAT<sup>®</sup> are those where *C. botulism* organism might continue to be present in the body and elaborating toxin, such as with:**
    - **Wound botulism**
    - **Adult intestinal colonization**
  - **Please consult with the Section of Epidemiology, CDC, or an infectious disease specialist PRIOR to using a second vial for specifics on dosing and intervals.**

**Report all suspected cases of botulism immediately to:  
Section of Epidemiology  
907-269-8000 during business hours  
1-800-478-0084 after hours**

## **Treatment Instructions for use of BAT<sup>®</sup> (Botulinum Antitoxin)**

**Botulism is both a medical and public health emergency. As soon as patients are stable, any suspected case of botulism should be immediately reported to the Alaska Section of Epidemiology:**

**call 907-269-8000 during business hours or 1-800-478-0084 after hours.**

In March 2013, FDA licensed the use of BAT<sup>®</sup> for use in managing cases of suspected botulism. Prior to this, the product (H-BAT) was under an investigational new drug (IND) protocol for treatment of suspected cases. BAT<sup>®</sup> contains antitoxins to treat botulism types A-G, including E, which is the most common type in Alaska. One vial of BAT<sup>®</sup> is supplied in this botulism treatment kit. This document contains specific instructions for using BAT<sup>®</sup>.

### **Overview of treatment plan**

1. Obtain clinical specimens (blood, stool, vomitus) for botulinum toxin testing.
2. Save suspected food.
3. Administer BAT<sup>®</sup> per package insert instructions. **Closely monitor patient for any symptoms of anaphylactic symptoms; have resuscitative measures available.**

### **Detailed, step-by-step instructions**

1. PRIOR to administration of BAT<sup>®</sup>, draw 15-20 cc of whole blood most often into multiple tubes; enough to result in 10cc of serum. Ask your laboratory to separate off the serum and hold the serum in the refrigerator pending instructions from the Section of Epidemiology (SOE).
2. Whenever possible, obtain stool, vomitus, and gastric contents for botulism testing. Send these clinical specimens to your laboratory and ask them to be held pending instructions from SOE.
3. Save any suspect food items brought to the hospital by the patient/family member(s). Food should be refrigerated, sent to your laboratory, and held pending instructions from SOE.
4. If BAT<sup>®</sup> is received frozen, it can be thawed expeditiously at 37°C (99°F) in a warm water bath (instead of in a refrigerator at 2°C–8°C [36°F–46°F]). See package insert for specific details on storage, handling and dilution into 0.9% Sodium Chloride Injection (USP) for infusion.
5. Sensitivity testing is no longer required; however, skin sensitivity testing should be considered for those patients at risk of acute hypersensitivity reaction. See package insert for details.
6. Administer the BAT<sup>®</sup> according to the package insert; procedures are summarized on the following page in Tables 1 and 2. One 20 ml vial of BAT<sup>®</sup> is considered an adult dose. **Children ≥17 years of age** should receive an adult dose. For **children <17 years**, consult

package insert for weight-based scaling of dose. In general for very young children (0-3 years old), it is advisable to consult a CDC botulism officer at 770-488-7100 (24/7 hotline); or for **infants (less than 1 year old)** consult the California Infant Botulism Program (510-231-7600).

- Note that administration with an in-line filter (pore size 15 microns or less) is *strongly recommended but not required*. Smaller pore size in-line filters such as 0.2 micron or 1.2 microns may be used but may result in slower infusion. If no in-line filters are available, consider using a filter needle to withdraw the contents out of BAT<sup>®</sup> vial.

**Table 1 BAT Dosing Guide and Intravenous Infusion Rate**

Patient Group	Dose	Starting Infusion Rate (first 30 minutes)	Incremental Infusion Rate if Tolerated (every 30 minutes)	Maximum Infusion Rate
Adults (≥ 17 years)	One vial	0.5 mL/min	Double the rate	2 mL/min
Pediatric (1 year to < 17 years)	20 – 100% of adult dose	0.01 mL/kg/min Do not exceed the adult rate.	0.01 mL/kg/min	0.03 mL/kg/min Do not exceed the adult rate
Infants (< 1 year)	10% of adult dose regardless of body weight	0.01 mL/kg/min	0.01 mL/kg/min	0.03 mL/kg/min

Calculate pediatric BAT dose by body weight according to Table 2.

**Table 2 Pediatric Dosing Guide for BAT Based on Salisbury Rule (1 Year to < 17 Years)**

Body Weight (kg)	Percent of Adult Dose <sup>*</sup> (%)
10-14	20 <sup>**</sup>
15-19	30
20-24	40
25-29	50
30-34	60
35-39	65
40-44	70
45-49	75
50-54	80
≥ 55	100

<sup>\*</sup>Dosing guide is based on the Salisbury Rule (1):

- Body weight ≤ 30 kg: 2x weight (kg) = % adult dose to administer
- Body weight > 30 kg: weight (kg) + 30 = % adult dose to administer

Do not exceed 1 vial dose regardless of body weight.

<sup>\*\*</sup> Minimum pediatric dose is 20% of adult dose. See Table 1 for infant dose.

- The data for administration of a second dose of BAT<sup>®</sup> during a single episode of botulism is limited. Antitoxin does **NOT** reverse paralysis but arrests its progression. Recovery follows the regeneration of new neuromuscular connections. Therefore, typically a second dose or

vial is not recommended as one vial of BAT<sup>®</sup> contains enough antitoxin to cover all “naturally” occurring foodborne botulism. Other exposures, such as with an intentional release, could have higher toxin loads; special treatment guidance will be given in those situations.

Clinical situations that may require an additional dose of BAT<sup>®</sup> are those where *C. botulism* organism might continue to be present in the body and elaborating toxin, such as with:

- Wound botulism
- Adult intestinal colonization

**Please consult with the Section of Epidemiology, CDC, or an infectious disease specialist PRIOR to using a second vial for specifics on dosing and intervals.**

9. Report all adverse reactions to Cangene Corporation (doing business as Emergent BioSolutions) the manufacturer of BAT<sup>®</sup> at 1-800-768-2304; or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).
10. Fax completed forms (found in PART B of this packet) within 7 days of completion of BAT<sup>®</sup> therapy (or hospital discharge) to the Alaska Section of Epidemiology at **907-563-7868**  
**ATTN: Infectious Diseases Program:**
  - CDC Botulism Case Report Form
  - CDC Clinical Outcome Report Form

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use BAT® safely and effectively. See full prescribing information for BAT®.

**BAT® [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) - (Equine)] Sterile Solution for Injection**  
Initial U.S. Approval: 2013

### RECENT MAJOR CHANGES

Dosage and Administration, Preparation (2.2) [09/2016]

### INDICATIONS AND USAGE

BAT [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) - (Equine)] is a mixture of immune globulin fragments indicated for the treatment of symptomatic botulism following documented or suspected exposure to botulinum neurotoxin serotypes A, B, C, D, E, F, or G in adults and pediatric patients.

The effectiveness of BAT is based solely on efficacy studies conducted in animal models of botulism.

### DOSAGE AND ADMINISTRATION

**For intravenous use only.**

Administer BAT by slow intravenous infusion after dilution 1:10 in normal saline at the dose recommended in the following table.

Patient Group	Dose	Starting Infusion Rate (first 30 minutes)	Incremental Infusion Rate if Tolerated (every 30 minutes)	Maximum Infusion Rate
Adults (≥ 17 years)	One vial	0.5 mL/min	Double the rate	2 mL/min
Pediatric (1 year to <17 years)	20 – 100% of adult dose	0.01 mL/kg/min Do not exceed the adult rate	0.01 mL/kg/min	0.03 mL/kg/min Do not exceed the adult rate
Infants (< 1 year)	10% of adult dose regardless of body weight	0.01 mL/kg/min	0.01 mL/kg/min	0.03 mL/kg/min

### DOSAGE FORMS AND STRENGTHS

Each single-use vial contains a minimum potency of:

- 4,500 Units (U) for serotype A antitoxin,
- 3,300 U for serotype B antitoxin,
- 3,000 U for serotype C antitoxin,
- 600 U for serotype D antitoxin,
- 5,100 U for serotype E antitoxin,
- 3,000 U for serotype F antitoxin, and
- 600 U for serotype G antitoxin

### CONTRAINDICATIONS

None.

### WARNINGS AND PRECAUTIONS

- Hypersensitivity reactions including anaphylaxis. Prepare for monitoring and management of allergic reactions (5.1).
- Delayed allergic reactions (serum sickness). Patient monitoring is recommended (5.2).
- Infusion reactions. Monitor and slow or interrupt infusion and administer treatment based on the severity of the reaction (5.3).
- Interference with non-glucose specific blood sugar testing systems. Use glucose-specific testing systems (5.4).
- BAT is made from equine plasma and may contain infectious agents e.g. viruses (5.5).

### ADVERSE REACTIONS

- The most common adverse reactions observed in ≥5 % of healthy volunteers in clinical trials were headache, nausea, pruritus, and urticaria (6.1).
- The most common adverse reactions reported in ≥1% of patients in a clinical study were pyrexia, rash, chills, nausea, and edema (6.1).
- One serious adverse reaction of hemodynamic instability was observed in one patient in the clinical study (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Emergent BioSolutions Canada Inc. at 1-800-768-2304 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### USE IN SPECIFIC POPULATIONS

- Pediatric: Limited safety data is available in the pediatric population. Dosing in pediatric patients is based on Salisbury Rule (8.4).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: [01/2018]

## FULL PRESCRIBING INFORMATION: CONTENTS\*

1	INDICATIONS AND USAGE	8.4	Pediatric Use
2	DOSAGE AND ADMINISTRATION	8.5	Geriatric Use
2.1	Dosage and Administration	11	DESCRIPTION
2.2	Preparation	12	CLINICAL PHARMACOLOGY
3	DOSAGE FORMS AND STRENGTHS	12.1	Mechanism of Action
4	CONTRAINDICATIONS	12.2	Pharmacodynamics
5	WARNINGS AND PRECAUTIONS	12.3	Pharmacokinetics
5.1	Hypersensitivity Reactions	13	NONCLINICAL TOXICOLOGY
5.2	Delayed Allergic Reactions (Serum Sickness)	13.2	Animal Toxicology and Pharmacology
5.3	Infusion Reactions	14	CLINICAL STUDIES
5.4	Interference with Blood Glucose Testing	15	REFERENCES
5.5	Transmissible Infectious Agents	16	HOW SUPPLIED/STORAGE AND HANDLING
6	ADVERSE REACTIONS	16.1	How Supplied
6.1	Clinical Trials Experience	16.2	Storage and Handling
6.2	Postmarketing Experience	17	PATIENT COUNSELING INFORMATION
6.3	Immunogenicity		
7	DRUG INTERACTIONS		
8	USE IN SPECIFIC POPULATIONS		
8.1	Pregnancy		
8.2	Lactation		

\*Sections or subsections omitted from the full prescribing information are not listed

## **FULL PRESCRIBING INFORMATION**

### **1 INDICATIONS AND USAGE**

BAT [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine)] is a mixture of immune globulin fragments indicated for the treatment of symptomatic botulism following documented or suspected exposure to botulinum neurotoxin serotypes A, B, C, D, E, F, or G in adults and pediatric patients.

The effectiveness of BAT is based on efficacy studies conducted in animal models of botulism.

### **2 DOSAGE AND ADMINISTRATION**

**BAT is for intravenous use only.**

#### **2.1 Dosage and Administration**

- Each vial of BAT contains a minimum potency for serotypes A, B, C, D, E, F, and G antitoxin [*see Dosage Forms and Strengths (3)*].
- For adult, pediatric, and infant patient groups, administer a dose of BAT according to Table 1. For details on pediatric dosing by body weight see Table 2.
- Administer all BAT doses after dilution 1:10 in normal saline by slow intravenous infusion according to the varying infusion rates in Table 1.
- Monitor vital signs throughout the infusion. If tolerated, the infusion rate can be increased incrementally up to the maximum infusion rate, and continued for the remainder of the administration. Decrease infusion rate if the patient develops discomfort or infusion-related adverse reactions.

**Table 1 BAT Dosing Guide and Intravenous Infusion Rate**

Patient Group	Dose	Starting Infusion Rate (first 30 minutes)	Incremental Infusion Rate if Tolerated (every 30 minutes)	Maximum Infusion Rate
Adults (≥ 17 years)	One vial	0.5 mL/min	Double the rate	2 mL/min
Pediatric (1 year to < 17 years)	20 – 100% of adult dose	0.01 mL/kg/min Do not exceed the adult rate.	0.01 mL/kg/min	0.03 mL/kg/min Do not exceed the adult rate
Infants (< 1 year)	10% of adult dose regardless of body weight	0.01 mL/kg/min	0.01 mL/kg/min	0.03 mL/kg/min

Calculate pediatric BAT dose by body weight according to Table 2.

**Table 2 Pediatric Dosing Guide for BAT Based on Salisbury Rule (1 Year to < 17 Years)**

Body Weight (kg)	Percent of Adult Dose*
10-14	20**
15-19	30
20-24	40
25-29	50
30-34	60
35-39	65
40-44	70
45-49	75
50-54	80
≥ 55	100

\*Dosing guide is based on the Salisbury Rule (1):

- Body weight ≤ 30 kg: 2x weight (kg) = % adult dose to administer
- Body weight > 30 kg: weight (kg) + 30 = % adult dose to administer

Do not exceed 1 vial dose regardless of body weight.

\*\* **Minimum pediatric dose is 20% of adult dose. See**

Table 1 for infant dose.

## 2.2 Preparation

1. Bring vial to room temperature.

- If frozen, thaw vial by placing in a refrigerator at 36 to 46 °F (2 to 8 °C) until the contents are thawed for approximately 14 hours.
  - Product can be thawed rapidly by placing at room temperature for one hour followed by a water bath at 98.6 °F (37 °C) until thawed.
  - Do not thaw this product in a microwave oven. Do not refreeze the vial.
2. Inspect vial to ensure there is no damage to the seal or vial. If damaged, discard the vial.
  3. Do not shake the vial during preparation to avoid foaming.
  4. Dilute 1:10 in 0.9% Sodium Chloride Injection, USP (saline) by adding BAT solution from the vial to the appropriate amount of saline in an IV bag. Do not use any other diluents. As the fill volume per vial varies by lot number (approximately 10 to 22 milliliters per vial), 90 to 200 milliliters of saline will be required. Withdraw the entire contents of the vial to obtain the total volume in the vial. If a partial vial is required (for pediatric dosing), the entire content of the vial should be withdrawn to ensure accurate calculation of the dosage [Table 2].
  5. Visually inspect the product for particulate matter and discoloration prior to administration. Do not use if the solution is turbid, cloudy, or contains particles other than a few translucent-to-white proteinaceous particulates.
  6. Use an intravenous line with constant infusion pump. Use a 15 micron sterile, non-pyrogenic, low protein binding in-line filter.
  7. BAT vials are for single use only and contain no preservative. Once punctured, use the vial contents to prepare the infusion bag and administer as soon as possible.
  8. Discard any unused portion.

### **3 DOSAGE FORMS AND STRENGTHS**

BAT is a sterile solution of purified F(ab')<sub>2</sub> plus F(ab')<sub>2</sub>-related immune globulin fragments derived from equine plasma, containing antitoxin activity to botulinum neurotoxins A, B, C, D, E, F, and G.

Each single-use vial, regardless of size or fill volume, contains a minimum antitoxin potency of:

- 4,500 U serotype A antitoxin,
- 3,300 U serotype B antitoxin,
- 3,000 U serotype C antitoxin,
- 600 U serotype D antitoxin,
- 5,100 U serotype E antitoxin,
- 3,000 U serotype F antitoxin, and
- 600 U serotype G antitoxin.

## **4 CONTRAINDICATIONS**

None.

## **5 WARNINGS AND PRECAUTIONS**

### **5.1 Hypersensitivity Reactions**

Severe hypersensitivity reactions, including anaphylactic and anaphylactoid reactions may occur following BAT administration. Patients who have had previous therapy with an equine-derived antivenom/antitoxin, with a history of hypersensitivity to horses, asthma, or hay fever are at a greater risk for developing severe hypersensitivity reactions to BAT. Administer BAT in a setting with appropriate equipment, medication, including epinephrine, and personnel trained in the management of hypersensitivity, anaphylaxis, and shock.

Monitor all patients for signs and symptoms of acute allergic reaction (e.g. urticaria, pruritus, erythema, angioedema, bronchospasm with wheezing or cough, stridor, laryngeal edema, hypotension, tachycardia) during and following the BAT infusion. In case of hypersensitivity reaction, discontinue BAT administration immediately and administer appropriate emergency care. Have immediately available medications such as epinephrine for emergency treatment of acute hypersensitivity reactions.

For patients at risk for hypersensitivity reaction, begin BAT administration at the lowest rate achievable (< 0.01 mL/min) and monitor.

### **5.2 Delayed Allergic Reactions (Serum Sickness)**

Delayed allergic reactions (serum sickness e.g. fever, urticarial or maculopapular rash, myalgia, arthralgia, and lymphadenopathy) may occur following BAT administration, typically 10-21 days after infusion. Monitor patients for signs and symptoms of delayed allergic reaction.

If a delayed allergic reaction (serum sickness) is suspected, administer appropriate medical care.

### **5.3 Infusion Reactions**

Chills, fever, headaches, nausea, and vomiting can be related to the rate of infusion. Arthralgia, myalgia and fatigue or vasovagal reactions may also develop. Carefully observe patients for the onset of these infusion reactions throughout the infusion period and immediately following an infusion.

Reduce the rate of infusion if the patient experiences infusion reactions and administer symptomatic therapy. If symptoms worsen, discontinue the infusion and administer appropriate medical care.

## 5.4 Interference with Blood Glucose Testing

The maltose contained in BAT can interfere with some types of blood glucose monitoring systems i.e. those based on glucose dehydrogenase pyrroloquinoline-quinone (GDH-PQQ) method. This can result in falsely elevated glucose readings and inappropriate administration of insulin, resulting in life-threatening hypoglycemia. Cases of true hypoglycemia may go untreated if the hypoglycemic state is masked by falsely elevated results [*see Drug Interactions (7)*].

## 5.5 Transmissible Infectious Agents

Because BAT is made from equine plasma, it may carry the risk of transmitting infectious agents e.g. viruses. The equine plasma pools are screened for the presence of certain infectious agents and the manufacturing process for BAT includes measures to inactivate and remove certain viruses [*see Description (11)*]. Despite these measures, such products can still potentially transmit disease. No cases of transmission of viral diseases have been associated with the use of BAT.

Report all infections thought by a physician to have been transmitted by BAT to Emergent BioSolutions Canada Inc. at 1-800-768-2304. Discuss the risks and benefits of this product with the patient or their legal guardian before administering it to the patient [*see Patient Counseling Information (17)*].

## 6 ADVERSE REACTIONS

The most common adverse reactions observed in  $\geq 5\%$  of healthy volunteers in clinical trials were headache, nausea, pruritus, and urticaria.

The most common adverse reactions reported in  $\geq 1\%$  of patients in a clinical study were pyrexia, rash, chills, nausea, and edema.

The following serious adverse reactions are discussed in detail in other sections of the labeling:

- Hypersensitivity reactions [*see Warnings and Precautions (5.1)*]
- Delayed allergic reactions/serum sickness [*see Warnings and Precautions( 5.2)*]
- Infusion reactions [*see Warnings and Precautions (5.3)*]

### 6.1 Clinical Trials Experience

*Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.*

In a randomized, double-blind, parallel arm trial conducted to evaluate the safety of BAT in healthy subjects, and to establish the pharmacokinetic profile of the seven botulinum antitoxin serotypes contained in BAT following intravenous (IV) administration, 40 subjects were randomized to receive either one (n=20) or two vials (n=20) of BAT.

In a second parallel arm, randomized, double-blind pharmacodynamic trial, 26 healthy subjects were randomized to receive either BAT in saline (n=16) or placebo (0.9% saline; n=10).

The most common adverse reactions in all healthy subjects were headache (9%), pruritus (5%), nausea (5%), and urticaria (5%). Other adverse reactions reported in less than 4% of subjects included pyrexia and throat discomfort. All reported adverse reactions were considered mild or moderate. No serious adverse reactions were reported. Two moderate acute allergic reactions that required premature termination of the infusion and treatment were reported. Reactions were predefined as mild if the subject was aware but could tolerate. Moderate reactions were predefined as discomfort enough to interfere with normal daily activity.

A total of 231 subjects with suspected or confirmed botulism were exposed to BAT in an open-label observational expanded access clinical study sponsored by the Centers for Disease Control and Prevention (CDC).

The majority of adult (213/216) and pediatric (13/15) subjects received one dose of BAT. Three adult subjects were exposed to a second dose of BAT, and two pediatric subjects each received two infant doses (10% of the adult dose). The administration of a second dose varied from seven hours to one month after the first dose.

Safety data was actively collected from treating physicians by the CDC. However, no on-site safety monitoring was performed, and the CDC relied on follow-up information provided by the treating physicians to determine the reporting frequencies for adverse reactions. Of the 231 subjects receiving BAT, safety information was available for 228 subjects. Adverse reactions were reported in 10% of all subjects. The most common adverse reactions were pyrexia (4%), rash (2%), chills (1%), nausea (1%), and edema (1%). Other adverse reactions were reported in less than 1% of subjects. No subject experienced anaphylaxis. One subject experienced a serious adverse reaction of hemodynamic instability characterized by bradycardia, tachycardia, and asystole during BAT administration. One subject experienced mild serum sickness (< 1%) with myalgia, arthralgia, and dark urine twelve days after BAT administration.

**Table 3 Summary of Adverse Drug Reactions (ADR) Reported in Subjects that Received BAT through the CDC Expanded Access Clinical Study**

System Organ Class	Preferred Term	Overall (N=228)		
		No. of Events	No. of Subjects	% of Subjects
ALL BODY SYSTEM	OVERALL	37	23	10.1
Cardiac disorders	Cardiac arrest	1	1	0.4
	Bradycardia	1	1	0.4
	Tachycardia	1	1	0.4
Gastrointestinal disorders	Vomiting	1	1	0.4
	Nausea	2	2	0.9

System Organ Class	Preferred Term	Overall (N=228)		
		No. of Events	No. of Subjects	% of Subjects
General disorders and administration site conditions	Pyrexia	9	9	3.9
	Chest discomfort	1	1	0.4
	Edema	2	2	0.9
	Chills	3	3	1.3
	Feeling jittery	1	1	0.4
Immune system disorders	Serum Sickness	1	1	0.4
Investigations	Blood pressure increased	1	1	0.4
	White blood cell count increased	1	1	0.4
Psychiatric disorders	Agitation	1	1	0.4
	Anxiety	1	1	0.4
Renal and urinary disorders	Urinary retention	1	1	0.4
Respiratory, thoracic and mediastinal disorders	Bronchospasm	1	1	0.4
Skin and subcutaneous tissue disorders	Erythema	1	1	0.4
	Hyperhidrosis	1	1	0.4
	Rash	4	4	1.8
Vascular disorders	Hemodynamic instability	1	1	0.4
	Hypotension	1	1	0.4

All adverse reactions were classified according to MedDRA Version 15.0 and are ranked according to medical significance within a given SOC.

## 6.2 Postmarketing Experience

The following hypersensitivity/allergic reactions have been reported in patients treated with BAT:

- Anaphylactic shock
- Angioedema
- Urticaria

## 6.3 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. All subjects from the two clinical trials were tested for immunogenicity against BAT at baseline and at the end of the studies (Day 28) using a validated assay. Eleven subjects seroconverted during the course of the two trials. One subject from each clinical trial experienced a moderate allergic reaction during the administration of BAT. Both subjects were negative for anti-BAT antibodies at baseline and at the end of their respective studies. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed

incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to BAT with the incidence of antibodies to other products may be misleading.

## **7 DRUG INTERACTIONS**

### *Drug Laboratory Interactions: Blood Glucose Testing*

BAT contains maltose which can interfere with certain types of blood glucose monitoring systems [see *Warnings and Precautions (5.4)*]. Only test systems that are glucose-specific should be used in patients receiving BAT. This interference can result in falsely elevated glucose readings that can lead to untreated hypoglycemia or to inappropriate insulin administration, resulting in life-threatening hypoglycemia.

The product information of the blood glucose testing system, including that of the test strips, should be carefully reviewed to determine if the system is appropriate for use with maltose-containing parenteral systems. If any uncertainty exists, contact the manufacturer of the testing system to determine if the system is appropriate for use with maltose-containing parenteral products.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### *Risk Summary*

There are no human or animal data to establish the presence or absence of BAT associated risk.

### **8.2 Lactation**

#### *Risk Summary*

There are no data to assess the presence or absence of BAT in human milk, the effects on the breastfed child, or the effects on milk production/excretion.

Consider the developmental and health benefits of breastfeeding along with the mother's clinical need for BAT and any potential adverse effects on the breastfed child from BAT or from the underlying maternal condition.

### **8.4 Pediatric Use**

The effectiveness of BAT has not been established in pediatric patients. Limited pediatric safety data are available.

Fifteen pediatric subjects (age 10 days to 17 years; including 1 newborn, 3 infants and toddlers, 4 children and 7 adolescents) received BAT under the CDC expanded access

clinical study. A 3-year old subject and an infant received two infant doses, and 13 pediatric subjects received one pediatric dose according to Salisbury Rule [Table 2].

Two adverse reactions were reported in two pediatric subjects. One subject experienced an adverse reaction of pyrexia following infusion of BAT, while the other subject experienced a serious adverse reaction of hemodynamic instability characterized by tachycardia, bradycardia, and asystole during infusion of BAT.

Dosing in pediatric patients is based on Salisbury Rule.

## 8.5 Geriatric Use

The safety, pharmacokinetics, and effectiveness of BAT have not been established in geriatric subjects.

Thirty six geriatric subjects received BAT under the CDC expanded access clinical study. One geriatric subject experienced rash as an adverse reaction following infusion of BAT.

## 11 DESCRIPTION

BAT [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine)] is a sterile solution of F(ab')<sub>2</sub> and F(ab')<sub>2</sub>-related antibody fragments prepared from plasma obtained from horses that have been immunized with a specific serotype of botulinum toxoid and toxin. To obtain the final heptavalent product, the seven antitoxin serotypes are blended. BAT is supplied in either a 20 or 50 milliliter vial size, with a fill volume ranging from 10 to 22 milliliters per vial. BAT is administered intravenously.

The manufacturing process for each antitoxin type includes cation-exchange chromatography to purify the immune globulin fraction, digestion with pepsin to produce F(ab')<sub>2</sub> plus F(ab')<sub>2</sub>-related immune globulin fragments, anion exchange chromatography to remove the pepsin as well as other impurities and filtration. In addition, the manufacturing process includes two viral inactivation/removal steps; solvent/detergent (S/D) treatment and virus filtration [Table 4].

The S/D treatment step is effective at inactivating known lipid-enveloped viruses such as equine encephalitis, equine arteritis, West Nile virus, equine infectious anemia, equine herpes virus, rabies, and equine influenza. The BAT manufacturing process also includes a robust filtration step that is effective in reducing the levels of some lipid-enveloped viruses (listed above) as well as non-enveloped viruses including equine rhinovirus, equine adenoviruses and adeno-associated viruses, and equine parvovirus.

**Table 4 Viral Clearance Capacity of the BAT Process**

Genome	Enveloped					Non-enveloped		
	RNA	RNA	RNA	DNA	RNA	DNA	DNA	RNA
Virus	XMuLV	WNV	BVDV	PRV	PI3	Ad2	Porcine Parvovirus	EMC
Family	Retro	Flavi	Flavi	Herpes	Paramyxo	Adeno	Parvo	Picorna

Size (nm)	Enveloped					Non-enveloped		
	80-110	40-70	50-70	150-200	100-200	70-90	18-24	25-30
Nanofiltration (log <sub>10</sub> )	≥ 2.7	≥ 2.1	≥ 4.5	n.t	n.t.	≥ 4.7	4.5	≥ 4.5
S/D (log <sub>10</sub> )	≥ 4.3	≥ 5.1	n.t.	≥ 5.1	≥ 5.5	n.t.	n.t.	n.t.
Total Reduction (log <sub>10</sub> )	≥ 7.0	≥ 7.2	≥ 4.5	≥ 5.1	≥ 5.5	≥ 4.7	4.5	≥ 4.5

XMuLV: Xenotropic Murine Leukemia Virus; specific model for equine infectious anemia, and a model for lipid-enveloped RNA viruses of similar size, such as vesicular stomatitis virus (Rhabdo family).

WNV: West Nile Virus; relevant virus, and specific model for lipid-enveloped RNA viruses, including the arboviruses, which contains both Flaviviridae and Togaviridae and includes equine encephalitis viruses (Toga family) and equine viral arteritis (Arteri family, formerly a Toga virus).

BVDV: Bovine Viral Diarrhea Virus; relevant virus, and specific model for lipid-enveloped RNA viruses, including the arboviruses, which contains both Flaviviridae and Togaviridae and includes equine encephalitis viruses (Toga family) and equine viral arteritis (Arteri family, formerly a Toga virus).

PRV: Pseudorabies Virus; specific model for equine herpes viruses and non-specific model for lipid-enveloped viruses.

PI3: Parainfluenza III Virus; model for lipid enveloped RNA viruses, and viruses of the similar family, orthomyxo, which includes equine influenza virus.

Ad2: Adenovirus; specific model for equine adenovirus.

EMC: Encephalomyocarditis Virus; specific model for equine parvovirus and adeno-associated virus, non-specific model for small lipid and non-lipid enveloped viruses.

n.t. – not tested

BAT is formulated with 10% maltose and 0.03% polysorbate 80. The formulated bulk material contains approximately 3-7 g% (30-70 milligrams/milliliter) protein.

The product potency is expressed in units based on the mouse neutralization assay (MNA). Each unit of BAT is designed to neutralize 10,000 mouse intraperitoneal lethal dose 50% units (MIPLD<sub>50</sub>) of botulinum neurotoxin for serotype A, B, C, D, F, and G and 1,000 MIPLD<sub>50</sub> of serotype E.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

The mechanism of action of BAT is through passive immunization with equine polyclonal antibody fragments (primarily F(ab')<sub>2</sub> and Fab) against botulinum neurotoxin (BoNT) A, B, C, D, E, F, and G. In the circulation the polyclonal antibody fragments bind to free BoNT. This prevents the BoNT from interacting with ganglioside anchorage sites and protein receptors on the cholinergic nerve endings. In turn this prevents BoNT internalization into the target cells. The antibody/antigen complexes are then cleared from the circulation by the organs involved in processing immune complexes.

Experimental evidence concerning the amount of circulating antitoxin needed to counteract BoNT intoxication is not fully documented. The outcome of treatment depends, as it does with other comparable conditions, largely on the time interval elapsing after the onset of symptoms and antitoxin administration.

## 12.2 Pharmacodynamics

A proof-of-concept clinical dose-response trial was conducted using the extensor digitorum brevis (EDB) muscle of the foot as a model for measuring muscle paralysis after exposure to botulism toxin. In this model, BAT prevented subjects from experiencing a decrease in muscle function after exposure to botulinum neurotoxin (BoNT) serotypes A and B. Subjects treated with placebo (n=10) demonstrated a loss of greater than 50% EDB muscle function within 3 days of exposure to BoNT serotypes A and B. In the BAT arm of the trial (n=16), EDB muscle function was stable over time indicating that BAT was effective in preserving muscle function for up to 28 days following exposure to both BoNT serotype A and B.

## 12.3 Pharmacokinetics

The pharmacokinetics (PK) of the seven botulism antitoxin serotypes was determined in healthy human subjects following IV administration of either one (n=20) or two vials (n=20) of BAT. The various PK parameters are summarized in Table 5.

The PK parameters varied based upon the antitoxin serotype measured. Antitoxin serotypes D and E had the shortest half-lives. While antitoxin serotype B and C had the longest half-lives. The AUC<sub>0-∞</sub> and C<sub>max</sub> values increased in a dose proportional fashion as the BAT dose increased from one to two vials. In addition, mean clearance values appeared to be similar between both treatment groups for the seven antitoxin serotypes, suggesting dose linearity of BAT over the dose range studied.

**Table 5 Pharmacokinetic Parameters (Mean) for Antitoxin Serotypes A Through G in Humans Following Intravenous Administration of either One or Two Vials of BAT**

Antitoxin Serotype	Treatment Group	AUC <sub>0-∞</sub> (U*hr/mL)	C <sub>max</sub> (U/mL)	t <sub>1/2</sub> (hr)	Cl (mL/hr)	V <sub>d</sub> (mL)
A	1 Vial	26.00	2.69	8.64	293	3637
	2 Vials	56.09	6.23	10.20	285	3993
B	1 Vial	29.30	1.90	34.20	196	9607
	2 Vials	62.55	4.28	57.10	181	14865
C	1 Vial	37.34	2.26	29.60	144	6066
	2 Vials	86.25	4.89	45.60	127	8486
D	1 Vial	7.62	0.81	7.51	137	1465
	2 Vials	14.83	1.60	7.77	151	1653
E	1 Vial	7.16	0.94	7.75	1250	14172
	2 Vials	15.66	1.75	7.32	1110	11596
F	1 Vial	31.40	2.37	14.10	169	3413
	2 Vials	63.19	4.29	18.20	168	4334

Antitoxin Serotype	Treatment Group	AUC <sub>0-∞</sub> (U*hr/mL)	C <sub>max</sub> (U/mL)	t <sub>1/2</sub> (hr)	Cl (mL/hr)	V <sub>d</sub> (mL)
G	1 Vial	7.05	0.59	11.70	149	2372
	2 Vials	14.66	1.19	14.70	144	3063

AUC = Area Under the Concentration Curve; Cl = Clearance; C<sub>max</sub> = Maximum Serum Concentration; BAT = Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine); t<sub>1/2</sub> = Half-life; T<sub>max</sub> = Time to Maximum Serum Concentration; U = Unit; V<sub>d</sub> = Volume of Distribution.

## 13 NONCLINICAL TOXICOLOGY

### 13.2 Animal Toxicology and Pharmacology

Toxicological studies were not conducted for BAT or its components.

The evaluation of new treatment options for botulism using controlled human trials is unethical and infeasible. Therefore the effectiveness of BAT for treatment of botulism is based on well controlled efficacy studies conducted in guinea pigs and rhesus macaques.

#### *Guinea Pig*

In a controlled therapeutic efficacy study, guinea pigs were intoxicated with various BoNT serotypes (A, B, C, D, E, F or G) at a dose of 1.5x guinea pig intramuscular lethal dose 50% units (GPIMLD<sub>50</sub>) via intramuscular injection into the right hind limb. The animals were then treated with either placebo control or 1x scaled human dose of BAT (weight/weight based on an average human body weight of 70 kilograms), after the onset of moderate clinical signs of botulism (right hind limb weakness, salivation, lacrimation, weak limbs and noticeable changes in breathing rate or pattern). Treatment with BAT resulted in a statistically significant improvement in the survival rate of animals across all of the serotypes tested [Table 6].

**Table 6 Summary of Guinea Pig Survival Data from BAT Therapeutic Efficacy Study**

Neurotoxin Serotype	Treatment Group	Survival Rate (%)	Two-sided Fisher's Exact Test (p-value)
A	1x BAT	34/34 (100%)	p<0.0001
	Placebo Control	0/34 (0%)	
B	1x BAT	34/34 (100%)	p<0.0001
	Placebo Control	1/34 (3%)	
C	1x BAT	33/34 (97%)	p<0.0001
	Placebo Control	4/34 (12%)	
D	1x BAT	33/34 (97%)	p<0.0001
	Placebo Control	5/34 (15%)	
E	1x BAT	34/34 (100%)	p<0.0001
	Placebo Control	0/34 (0%)	
F	1x BAT	34/34 (100%)	p<0.0001
	Placebo Control	4/34 (12%)	

Neurotoxin Serotype	Treatment Group	Survival Rate (%)	Two-sided Fisher's Exact Test (p-value)
G	1x BAT	34/34 (100%)	p<0.0001
	Placebo Control	17/34 (50%)	

BAT = Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine).

### *Nonhuman Primate*

In a controlled therapeutic efficacy study, rhesus macaques were intoxicated with BoNT serotype A delivered intravenously at a dose of 1.7x nonhuman primate intravenous lethal dose 50% (NHPLD<sub>50</sub>) units per kilogram of body weight. The animals were then treated with either placebo control or 1x scaled human dose of BAT (weight/weight based on an average human body weight of 70 kilograms), after the onset of clinical signs of botulism (ptosis, muscular weakness, or respiratory distress). Treatment with BAT resulted in a statistically significant improvement in the survival rate [Table 7].

**Table 7 Summary of Rhesus macaque Survival Data from BAT Therapeutic Efficacy Study**

Treatment Group	Survival Rate (%)	Two-sided Fisher's Exact Test (p-value)
1x BAT	14/30 (47%)	p<0.0001
Placebo Control	0/30 (0%)	

BAT = Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine).

## **14 CLINICAL STUDIES**

The effectiveness of BAT is based on efficacy studies demonstrating a survival benefit in animal models of botulism [*see Nonclinical Toxicology (13.2)*]. The safety has been tested in healthy adults and patients with suspected botulism who were treated with BAT under an expanded access clinical study.

The pharmacokinetic, pharmacodynamic, and safety profiles of BAT have been evaluated in two clinical studies. In these clinical studies, BAT was shown to have an acceptable safety profile when one or two vials of BAT were administered intravenously to healthy subjects.

In a randomized, single-center, double-blind trial the pharmacokinetics and safety of BAT was evaluated in 40 healthy subjects receiving either one (n = 20) or two (n = 20) vials of BAT by IV infusion. Serum BAT levels were measured in the subjects using the Mouse Neutralization Assay (MNA) [*see Clinical Pharmacology (12.3)*].

In a randomized single center, double-blind trial the pharmacodynamics and safety of BAT was evaluated in 26 healthy subjects receiving either a single vial of BAT (n=16) or placebo (n=10) by IV infusion. The effects of BAT in preventing paralysis of the EDB foot muscle following administration of botulinum neurotoxin serotype A or B was determined [*see Clinical Pharmacology (12.2)*].

To provide additional support for the efficacy demonstrated in the animal models, a preliminary analysis of data from a Centers for Disease Control and Prevention (CDC) open-

label, observational expanded access clinical study for the treatment of subjects with suspected or confirmed botulism with BAT was conducted. Across the 148 subjects treated with BAT in the period analyzed, 109 subjects had a final discharge diagnosis of suspected or confirmed botulism and were included in the analysis population. The median time from the onset of botulism symptoms to treatment with BAT was 3.6 days (range: 0.25 – 38 days). Early treatment ( $\leq 2$  days after onset of symptoms) with BAT was associated with a shorter length of hospitalization, duration in intensive care unit (ICU) and duration of mechanical ventilation compared to later treatment [Table 8] and is consistent with the mechanism of action [see *Clinical Pharmacology (12.1)*].

**Table 8 Summary of Duration of Hospitalization, ICU Stay and Mechanical Ventilation for CDC Patients Treated with BAT**

	<b>Time from Symptoms to Treatment</b>	<b>Number of Patients (N)</b>	<b>Mean Duration in Days (SD)</b>
Hospitalization	$\leq 2$ Days	14	12.4 (9.28)
	$> 2$ Days	72	26.1 (26.37)
ICU Stay	$\leq 2$ Days	13	9.2 (7.40)
	$> 2$ Days	70	15.8 (18.76)
Mechanical Ventilation	$\leq 2$ Days	9	11.6 (7.83)
	$> 2$ Days	41	23.4 (21.11)

## 15 REFERENCES

1. Lack JA, Stuart-Taylor ME. Calculation of drug dosage and body surface area of children. *Br J Anaesth.* 1997; 78:601-605.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 How Supplied

BAT is supplied in either 20 milliliter or 50 milliliter glass vials seated with a butyl rubber stopper and an aluminum seal with a plastic flip-top cap, with a fill volume ranging from 10 to 22 milliliters per vial. Each vial, regardless of size or fill volume contains a minimum potency of  $> 4,500$  U serotype A antitoxin,  $> 3,300$  U serotype B antitoxin,  $> 3000$  U serotype C antitoxin,  $> 600$  U serotype D antitoxin,  $> 5,100$  U serotype E antitoxin,  $> 3,000$  U serotype F antitoxin, and  $> 600$  U serotype G antitoxin.

BAT is not made with natural rubber latex.

<b>NDC Number</b>	<b>Product Description</b>
<b>60492-0075-2</b>	A 50 milliliter single dose vial.
<b>60492-0075-3</b>	A 20 milliliter single dose vial.

## 16.2 Storage and Handling

- Store frozen at or below  $\leq 5^{\circ}\text{F}$  ( $\leq -15^{\circ}\text{C}$ ) until used.
- Once thawed, Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine) may be stored at  $2-8^{\circ}\text{C}$  ( $36-48^{\circ}\text{F}$ ) for a maximum of 36 months or until 48 months from the date of manufacture, whichever comes first. Do not refreeze.
- Once punctured, use the vial contents to prepare the infusion bag and administer as soon as possible.
- BAT vials are for single use only and contain no preservative. Discard any unused portion.

## 17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information).

- Inform patients of the following:
  - BAT is prepared from equine plasma and may contain infectious agents such as viruses that can cause disease.
  - The risk that such products will transmit an infectious agent has been reduced by screening the horses for prior exposure to certain viruses, by testing for the presence of certain current viral infections, and by inactivating and/or removing certain viruses during manufacturing.
  - Despite these measures, such products can still potentially transmit disease.
  - There is also the possibility that unknown infectious agents may be present in such products.
- Inform patients that persons who have received previous therapy with an equine-derived antivenom/antitoxin, have known allergies to horses, have asthma or get hay fever (seasonal allergies) may be at increased risk of hypersensitivity reactions and should only receive BAT if the benefits outweigh the risks.
- Advise patients about the potential interference with non-glucose specific monitoring systems.
  - The maltose contained in BAT can interfere with some types of blood glucose monitoring systems.
  - Only testing systems that are glucose-specific should be used in patients receiving BAT.
  - This interference can result in falsely elevated glucose readings that can lead to untreated hypoglycemia or to inappropriate insulin administration, resulting in life-threatening hypoglycemia.

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**Manufactured by:**

Emergent BioSolutions Canada Inc.

155 Innovation Drive

Winnipeg, Manitoba

Canada, R3T 5Y3

U.S. License No. 2084

## PATIENT INFORMATION

BAT® [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine)]

### What is botulism?

Botulism is a muscle-paralyzing disease caused by a toxin made by a bacterium called *Clostridium botulinum*.

Botulism can cause the following conditions:

- Double vision,
- Blurred vision,
- Drooping eyelids,
- Slurred speech,
- Difficulty swallowing,
- Dry mouth,
- Muscle weakness that spreads through the body,
- Difficulty breathing.

Botulism can also cause paralysis and death. After a person is exposed to the toxin, problems can start as early as three hours or as late as a few days. It can take weeks or months to get better. During that time, many people need special care in the hospital.

The effectiveness of BAT has been studied in animals with botulism.

### What is BAT?

BAT is a botulism antitoxin made from the plasma of horses. It contains antibody fragments which can neutralize botulism toxins. BAT may make the illness from botulism less severe. Treatment with BAT will not reverse the paralysis, but may decrease the duration and extent of paralysis.

### Who should use BAT?

Your doctor may give you BAT if they suspect that you have been exposed to botulism toxin. You should get the treatment as quickly as possible to stop the progression of the illness.

Unless the benefits outweigh the risks, you should not receive BAT if you have a known history of allergies to horses or horse blood products, asthma or hay fever (seasonal allergies).

### How will you receive BAT?

BAT is given as an injection into your vein. Your doctor will determine the dose of BAT. The treatment may take several hours to administer. Your doctor will decide if you need more than one injection.

## **What are the possible or reasonably likely side effects of BAT?**

The most common side effects of BAT are:

- Headache
- Fever
- Rash
- Hives
- Chills
- Nausea
- Swelling

Some people have a chilly feeling, difficulty breathing, and have a quick rise in body temperature within the first 20 to 60 minutes after getting BAT. This can be managed by your doctor.

BAT can cause allergic reactions. Tell your doctor or go to the emergency department right away if you have trouble breathing, swelling of your tongue or lips, or a very fast heart rate because this can be signs of a serious allergic reaction.

Tell your doctor if you get pains in your joints and back, fever, and a rash within one to three weeks after getting BAT. These can be signs of “serum sickness” and can last for a few weeks. Your doctor can give you medicine to help with serum sickness.

Talk to your doctor about any side effects that concern you. You can ask your doctor for additional prescribing information that is available to healthcare professionals.

## **What other information do you need to know about BAT?**

BAT is made from horse plasma. The horses are carefully screened and the plasma is carefully cleaned, but there is a small risk that it may give you a virus. Talk to your doctor if you have any symptoms that concern you.

You may report side effects directly to Emergent BioSolutions Canada Inc. at 1-800-768-2304 or to the FDA’s MedWatch reporting system at 1-800-FDA-1088.

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### **Manufactured By:**

Emergent BioSolutions Canada Inc.  
155 Innovation Drive  
Winnipeg, Manitoba  
Canada, R3T 5Y3

US License No. 2084

# **BAT<sup>®</sup> (Botulinum Antitoxin) Kit Packing List**

## **PART B – FORMS\***

- Botulism Case Report Form
- Clinical Outcome Report Form to be completed by clinician administering BAT<sup>®</sup> and to be accompanied by a copy of the discharge summary

**Report all suspected cases of botulism immediately to:  
Section of Epidemiology  
907-269-8000 during business hours  
1-800-478-0084 after hours**

**\*Please return completed forms to Section of Epidemiology  
by fax 907-563-7868;  
or mail to  
Infectious Diseases Program / Section of Epidemiology  
3601 C Street, Suite 540, Anchorage, AK 99503**

## BOTULISM CASE REPORT

### REPORTING AGENCY

Officer Releasing Antitoxin		Health Agency		Telephone Number	Today's Date / /
Date of First Report / /	First Reported By		State Contact (if applicable)		
Treating Physician/Contact for H-BAT Release Name- <small>Last Name, First Name</small>		Telephone Number	Fax Number	Specialty <input type="checkbox"/> Internist <input type="checkbox"/> Intensivist <input type="checkbox"/> Neurologist <input type="checkbox"/> Infectious Disease <input type="checkbox"/> Pediatrician <input type="checkbox"/> Other _____	
Attending Physician Name - Last Name, First Name		Telephone Number	Fax Number	Specialty <input type="checkbox"/> Internist <input type="checkbox"/> Intensivist <input type="checkbox"/> Neurologist <input type="checkbox"/> Infectious Disease <input type="checkbox"/> Pediatrician <input type="checkbox"/> Other _____	
			Email		
			Email		

### DEMOGRAPHIC INFORMATION

Patient Name - Last Name, First Name, Middle Initial:		Patient's Telephone Number	Patient's E-mail Address		
Patient's Street Address		City	State	Zip Code	
Date of Birth / /	Age <input type="checkbox"/> Months <input type="checkbox"/> Years	Sex <input type="checkbox"/> Male <input type="checkbox"/> Female	Ethnicity <input type="checkbox"/> Non-Hispanic/Non-Latino <input type="checkbox"/> Hispanic/Latino <input type="checkbox"/> Unknown	Race (check all that apply) <input type="checkbox"/> Asian <input type="checkbox"/> Alaska Native <input type="checkbox"/> African-American/Black <input type="checkbox"/> Pacific Islander <input type="checkbox"/> Other _____ <input type="checkbox"/> American Indian <input type="checkbox"/> White <input type="checkbox"/> Unknown	

### CLINICAL INFORMATION

Symptomatic? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	Onset Date of First Botulism Symptom / /	Onset Hour (military) : :	Onset Date of Neurologic Symptoms / /	Date First Sought Medical Care / /	Currently Hospitalized? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	If yes, Admit date / /
Hospital Name		City		State	Zip Code	Telephone Numbers
Admitted to ICU? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk If yes, date / /		Placed on Ventilator? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk If yes, date / /		Additional Hospital Phone Numbers (e.g., Pharmacy and ICU)		

### CLINICAL PRESENTATION

Vital Signs (upon presentation)  
 Temperature (°F) \_\_\_\_\_ Blood Pressure (mmHg) \_\_\_\_/\_\_\_\_ Heart Rate (beats/min.) \_\_\_\_\_ Respiration Rate (breaths/min.) \_\_\_\_\_

Symptoms	Symptoms			Physical Exam Findings	Physical Exam Findings		
	Yes	No	Unk		Yes	No	Unk
Nausea				Alert and Oriented			
Vomiting				Extraocular Palsy (paralysis of eye muscles)			
Abdominal Pain				If yes, is it bilateral?			
Diarrhea				If bilateral, is it symmetric?			
Constipation				Ptosis (drooping eyelids)			
Blurred Vision				If yes, is it bilateral?			
Diplopia (double vision)				If bilateral, is it symmetric?			
Dizziness				Pupils dilated (mm= )			
Slurred Speech				If yes, is it bilateral?			
Thick tongue				Pupils constricted (mm= )			
Change in sound of voice				If yes, is it bilateral?			
Hoarseness				Pupils non-reactive			
Dry mouth				If yes, is it bilateral?			
Dysphagia (difficulty swallowing)				Facial Paralysis			
Shortness of breath				If yes, is it bilateral?			
Subjective weakness				If bilateral, is it symmetric?			
Fatigue				Palatal weakness			
Paresthesia (abnormal sensation, e.g. numbness)				If yes, is it bilateral?			
Urinary Retention				Impaired gag reflex			
Other Symptoms (specify):				Sensory deficit(s) If yes, specify			
				Other (specify):			

Comments / Remarks:

**Musculoskeletal Exam:** (0=no evidence of contractility; 1=slight contractility, no movement; 2=full range of motion, gravity eliminated; 3=full range of motion w/ gravity; 4=full range of motion against gravity, some resistance; 5=full range of motion against gravity, full resistance)

Proximal Upper Extremity R: \_\_\_/5    Distal Upper Extremity R: \_\_\_/5    Proximal Lower Extremity R: \_\_\_/5    Distal Lower Extremity R: \_\_\_/5  
 L: \_\_\_/5    L: \_\_\_/5    L: \_\_\_/5    L: \_\_\_/5  
Unk    Unk    Unk    U

**Deep Tendon Reflexes:** (0=No response; 1=sluggish or diminished; 2=active or expected response; 3=more brisk than expected, slightly hyperactive; 4=brisk, hyperactive, with intermittent or transient clonus)

Biceps/Triceps R: \_\_\_/4    Brachial R: \_\_\_/4    Patellar R: \_\_\_/4    Ankle R: \_\_\_/4  
 L: \_\_\_/4    L: \_\_\_/4    L: \_\_\_/4    L: \_\_\_/4  
Unk    Unk    Unk    Unk

**If muscle weakness/paralysis present, describe progression.**

Ascending, ending with cranial nerves    Descending, beginning with cranial nerves    Other: \_\_\_\_\_

**Clinical Tests**    Yes No Unk If yes, specify as noted

Lumbar puncture CSF analysis	Date ___/___/___	Repeat Lumbar puncture?	Date ___/___/___
	WBC count _____	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	WBC count _____
	RBC _____	If yes, specify as noted	RBC _____
	Glucose _____		Glucose _____
	Protein _____		Protein _____
EMG	Date ___/___/___	Done with rapid, repetitive stimulation	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk    If yes, at what hertz? _____
		Check one:	<input type="checkbox"/> Suggestive of/consistent with botulism <input type="checkbox"/> Not consistent with botulism <input type="checkbox"/> Unk
Edrophonium (Tensilon)	Date ___/___/___	Describe test results: _____	
CT scan or MRI scan	<input type="checkbox"/> Head <input type="checkbox"/> Spine <input type="checkbox"/> Other _____	Suggestive of diagnosis other than botulism <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	
	Describe: _____		

**Past Medical History**

Prior Botulism Diagnosis? Yes No Unk    If yes, date \_\_\_/\_\_\_/\_\_\_

Medications that could cause neuromuscular paralysis used within 30 days before illness onset (check all that apply):  
Myobloc (toxin type B)    Aminoglycoside (e.g. gentamicin, tobramycin)    Other \_\_\_\_\_  
Botox (toxin type A)    Anticholinergic    Other \_\_\_\_\_

Prior Neurologic Impairment? Yes No Unk    If yes, specify \_\_\_\_\_

Does the patient have an allergy to equine products? Yes No Unk    If yes, describe \_\_\_\_\_

**Differential Diagnosis per attending MD** (Please place a 1 for the most likely diagnosis, 2 for the second most likely, and 3 for the third most likely)

\_\_\_ Botulism    \_\_\_ Tick paralysis    \_\_\_ Paralytic shellfish poisoning  
 \_\_\_ Myasthenia gravis    \_\_\_ Eaton-Lambert syndrome    \_\_\_ Other \_\_\_\_\_  
 \_\_\_ Guillain-Barré syndrome    \_\_\_ Stroke or central nervous system mass or lesion    \_\_\_ Other \_\_\_\_\_

**EPIDEMIOLOGIC INFORMATION**

**Travel History**

Did patient travel **outside county of residence** within 15 days prior to illness onset?    Yes No Unk

If yes, specify all locations and dates below.

Location (city, county, state, country)	Dates of Travel
_____	___/___/___ to ___/___/___
_____	___/___/___ to ___/___/___
_____	___/___/___ to ___/___/___

**Contacts/ Other Ill Persons**

Any contacts with similar illness?    Yes No Unk    If yes, complete table below.

Name	Age	City, State	Onset Date	Relationship
			___/___/___	
	Sex	Telephone Number	Date Reported to Public Health	Nature of Contact
	( )	( )	___/___/___	
Name	Age	City, State	Onset Date	Relationship
			___/___/___	
	Sex	Telephone Number	Date Reported to Public Health	Nature of Contact
	( )	( )	___/___/___	

Comments / Remarks:

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

**Exposures / Risk Factors**

Provide information about the patient's wound and drug use in the table below.

	Yes	No	Unk	If yes, specify as noted
Wound or Abscess				Location(s): Description: Date of injury: ___/___/___ How wound occurred: Did/does wound appear infected? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk
Injects Black Tar Heroin (Chiba)				Date last used: ___/___/___ Injection method (check all that apply): <input type="checkbox"/> Intravenous <input type="checkbox"/> Intramuscular <input type="checkbox"/> Subcutaneous (skin-pop) <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk
Injects other drugs				Drugs injected (check all that apply): <input type="checkbox"/> Heroin <input type="checkbox"/> Cocaine <input type="checkbox"/> Methamphetamine <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk Injection method (check all that apply): <input type="checkbox"/> Intravenous <input type="checkbox"/> Intramuscular <input type="checkbox"/> Subcutaneous (skin-pop) <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk
Sniffs/snorts drugs				Drugs sniffed/snorted (check all that apply): <input type="checkbox"/> Heroin <input type="checkbox"/> Cocaine <input type="checkbox"/> Methamphetamine <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk
Uses other drugs				Types:

Provide information regarding any suspect food items consumed prior to illness in the table below. If more than three items, append pages; please ask about high risk foods even if wound botulism is suspected. Please pay special attention to fish or seafood exposures.

	Suspect Food 1	Suspect Food 2	Suspect Food 3
Food item			
Date and time eaten	Date: ___/___/___ Time: ___:___ am/pm	Date: ___/___/___ Time: ___:___ am/pm	Date: ___/___/___ Time: ___:___ am/pm
Type of item (check one)	<input type="checkbox"/> Homemade <input type="checkbox"/> Commercial product • Brand: _____ • Lot number: _____ <input type="checkbox"/> Restaurant-associated <input type="checkbox"/> Unk	<input type="checkbox"/> Homemade <input type="checkbox"/> Commercial product • Brand: _____ • Lot number: _____ <input type="checkbox"/> Restaurant-associated <input type="checkbox"/> Unk	<input type="checkbox"/> Homemade <input type="checkbox"/> Commercial product • Brand: _____ • Lot number: _____ <input type="checkbox"/> Restaurant-associated <input type="checkbox"/> Unk
How item preserved	<input type="checkbox"/> Canned <input type="checkbox"/> Dried <input type="checkbox"/> Fermented <input type="checkbox"/> Salted <input type="checkbox"/> Pickled <input type="checkbox"/> No preservation <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk	<input type="checkbox"/> Canned <input type="checkbox"/> Dried <input type="checkbox"/> Fermented <input type="checkbox"/> Salted <input type="checkbox"/> Pickled <input type="checkbox"/> No preservation <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk	<input type="checkbox"/> Canned <input type="checkbox"/> Dried <input type="checkbox"/> Fermented <input type="checkbox"/> Salted <input type="checkbox"/> Pickled <input type="checkbox"/> No preservation <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk
How item stored	<input type="checkbox"/> Unrefrigerated <input type="checkbox"/> Refrigerated <input type="checkbox"/> Frozen <input type="checkbox"/> Unk <input type="checkbox"/> Other: _____	<input type="checkbox"/> Unrefrigerated <input type="checkbox"/> Refrigerated <input type="checkbox"/> Frozen <input type="checkbox"/> Unk <input type="checkbox"/> Other: _____	<input type="checkbox"/> Unrefrigerated <input type="checkbox"/> Refrigerated <input type="checkbox"/> Frozen <input type="checkbox"/> Unk <input type="checkbox"/> Other: _____
How item served	<input type="checkbox"/> Heated <input type="checkbox"/> Only warmed <input type="checkbox"/> Unheated <input type="checkbox"/> Fried <input type="checkbox"/> Boiled <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk	<input type="checkbox"/> Heated <input type="checkbox"/> Only warmed <input type="checkbox"/> Unheated <input type="checkbox"/> Fried <input type="checkbox"/> Boiled <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk	<input type="checkbox"/> Heated <input type="checkbox"/> Only warmed <input type="checkbox"/> Unheated <input type="checkbox"/> Fried <input type="checkbox"/> Boiled <input type="checkbox"/> Other: _____ <input type="checkbox"/> Unk
# persons sharing item			
# persons ill			
Samples of food available	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk
Samples submitted for botulism testing	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk
Foods of same lot/batch recovered or recalled	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk

Provide information regarding any other exposures of interest in the table below.

Exposure	Description

# Clinical Outcome Report\*

*\*Please include copy of discharge summary*

**Please complete upon discharge or death and fax to 907-563-7868 ATTN: Botulism Surveillance**

REPORTING AGENCY			
Treating Physician - Last Name, First Name	Telephone Number	Fax Number	Today's Date ____/____/____
Attending Physician Name - Last Name, First Name	Telephone Number	Fax Number	Speciality
Hospital Name	City	State	Zip Code
DEMOGRAPHIC INFORMATION			
Patient Name - Last Name, First Name, Middle Initial	City	State	Zip Code
Date of Birth ____/____/____	Sex <input type="checkbox"/> Male <input type="checkbox"/> Female		
CLINICAL OUTCOME INFORMATION			
How many days was patient hospitalized? _____ days			
How many days was patient in intensive care? _____ days			
Did patient require mechanical ventilation?		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	
If yes, how many days was patient on a ventilator? _____ days			
Did patient require a tracheostomy?		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	
If yes, when was the tracheostomy done? ____/____/____			
Did the patient develop pneumonia?		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	
What was the final diagnosis? (please check one)			
<input type="checkbox"/> Botulism <input type="checkbox"/> Tick paralysis <input type="checkbox"/> Paralytic shellfish poisoning <input type="checkbox"/> Myasthenia gravis <input type="checkbox"/> Eaton-Lambert syndrome <input type="checkbox"/> Other _____ <input type="checkbox"/> Guillain-Barre syndrome <input type="checkbox"/> Stroke or central nervous system mass or lesion			
Was treatment given for any of the above diagnosis (even if it wasn't the final diagnosis)? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk			
If yes, specify type <input type="checkbox"/> Botulism Antitoxin <input type="checkbox"/> Plasmapheresis <input type="checkbox"/> Neostigmine/Physostigmine <input type="checkbox"/> Other Immunoglobulin therapy _____			
Did the patient develop an adverse event after botulism antitoxin administration?		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	
If yes, specify adverse event _____			
Did the patient die?		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	
If yes, When did patient die? ____/____/____			
What was the cause of death? _____			
If no, Where was patient discharged? <input type="checkbox"/> Home <input type="checkbox"/> Nursing home <input type="checkbox"/> Physical therapy/rehabilitation facility <input type="checkbox"/> Other (specify) _____			
Did patient have residual disability upon discharge?		<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	
<b>If yes, please specify types below (check as many as apply)</b>			
<input type="checkbox"/> Proximal Upper Extremity Weakness <input type="checkbox"/> Diminished deep tendon reflexes <input type="checkbox"/> Other _____ <input type="checkbox"/> Distal Upper Extremity Weakness <input type="checkbox"/> Fatigue <input type="checkbox"/> Other _____ <input type="checkbox"/> Proximal Lower Extremity Weakness <input type="checkbox"/> Stroke or central nervous system mass or lesion <input type="checkbox"/> Distal Lower Extremity Weakness <input type="checkbox"/> Other _____			
ADDITIONAL INFORMATION			
Comments / Remarks:			