

Product Monograph
Including Patient Medication Information

BAT[®]

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

Sterile Solution for Injection

4500 U serotype A antitoxin, 3300 U serotype B antitoxin, 3000 U serotype C antitoxin, 600 U serotype D antitoxin, 5100 U serotype E antitoxin, 3000 U serotype F antitoxin, and 600 U serotype G antitoxin per vial.

Immune Sera and Immunoglobulin

ATC code: J06AA04

“HEALTH CANADA HAS AUTHORIZED THE SALE OF THIS EXTRAORDINARY USE NEW DRUG FOR DOCUMENTED OR SUSPECTED EXPOSURE TO BOTULINUM NEUROTOXIN SEROTYPES A, B, C, D, E, F, or G BASED ON LIMITED CLINICAL TESTING IN HUMANS”

Emergent BioSolutions Canada Inc.

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Recent Major Label Changes

| | |
|----------------|-----------|
| Not Applicable | [MM/YYYY] |
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Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

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Part 1: Healthcare Professional Information

“HEALTH CANADA HAS AUTHORIZED THE SALE OF THIS EXTRAORDINARY USE NEW DRUG FOR DOCUMENTED OR SUSPECTED EXPOSURE TO BOTULINUM NEUROTOXIN SEROTYPES A, B, C, D, E, F, or G BASED ON LIMITED CLINICAL TESTING IN HUMANS”

1. Indications

BAT[®] [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine)] is 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 demonstrating survival benefit in animal models of botulism.

1.1. Pediatrics

Pediatrics (<17 years of age): The effectiveness of BAT has not been established in pediatric patients. Limited pediatric safety data are available (for more information see [7 Warnings and Precautions](#), [7.1 Special Populations](#), [7.1.3 Pediatrics](#)).

1.2. Geriatrics

Geriatrics (>65 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatrics use.

2. Contraindications

There is no contraindication to the use of BAT if indicated following exposure to botulinum neurotoxin.

See **Warnings and Precautions**, patients 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, and patients should be closely monitored with resuscitative measures available, during and following administration.

3. Serious Warnings and Precautions Box

- Prepare for monitoring and management of hypersensitivity reactions, infusion reactions or delayed allergic reactions (serum sickness) (See [7 Warnings and Precautions](#))
- BAT is prepared using pools of equine plasma, therefore may carry the risk of transmitting infectious agents (see [7 Warnings and Precautions](#))

4. Dosage and Administration

4.1. Dosing Considerations

BAT is for intravenous use only.

4.2. Recommended Dose and Dosage Adjustment

BAT is a sterile solution of purified F(ab')₂ and F(ab')₂-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 of BAT contains a minimum potency for serotypes A, B, C, D, E, F, and G antitoxin (see [6 Dosage Forms, Strengths, Composition, and Packaging, Table 3](#)).

For adult, pediatric and infant patient groups, administer a dose of BAT intravenously 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.

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

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 B\AT 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:

Body weight ≤ 30 kg: $2 \times \text{weight (kg)} = \% \text{ adult dose to administer}$

Body weight > 30 kg: $\text{weight (kg)} + 30 = \% \text{ adult dose to administer}$

Do not exceed 1 vial dose regardless of body weight.

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

4.4. Administration

1. Bring vial to room temperature prior to use.
 - 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 37 °C (98.6 °F) 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.
 - Do not shake the vial during preparation to avoid foaming.
3. 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 (ranging from 10 to 26 milliliters per vial), 90 to 235 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 (see [Table 2](#)).
4. Visually inspect the product for particulate matter and discoloration prior to administration. Do not use if the solution is turbid or contains particulates other than translucent-to-white proteinaceous particulates.
5. Use an intravenous line with constant infusion pump. Use a sterile, non-pyrogenic, low

protein binding in line filter.

6. 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.
7. Discard any unused portion.

5. Overdosage

For management of a suspected drug overdose, contact your regional Poison Control Centre.

6. Dosage Forms, Strengths, Composition, and Packaging

To help ensure the traceability of biologic products, health professionals should record both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 3 Dosage Forms, Strengths, and Composition

| Route of Administration | Dosage Form/ Strength / Composition | Non-Medicinal Ingredients |
|-------------------------|---|---------------------------|
| Intravenous | Sterile Solution for Injection. Each single-use vial contains a minimum potency of: <ul style="list-style-type: none">• 4500 U serotype A antitoxin,• 3300 U serotype B antitoxin,• 3000 U serotype C antitoxin,• 600 U serotype D antitoxin,• 5100 U serotype E antitoxin,• 3000 U serotype F antitoxin, and• 600 U serotype G antitoxin. | maltose polysorbate 80 |

Dosage Form and Packaging: BAT is supplied in 50 mL glass vials sealed with a rubber stopper and a plastic cap, with a fill volume ranging from 10 to 26 milliliters per vial. Each vial, regardless of size or fill volume, contains a minimum potency of >4500 U serotype A antitoxin, >3300 U serotype B antitoxin, >3000 U serotype C antitoxin, >600 U serotype D antitoxin, >5100 U serotype E antitoxin, >3000 U serotype F antitoxin, and >600 U serotype G antitoxin.

BAT is not made with natural rubber latex.

Composition: BAT is a sterile solution for intravenous injection. It is made of purified antibody fragments produced from equine immunoglobulins (IgGs) modified by pepsin digestion. Non-medicinal ingredients include 10% maltose and 0.03% polysorbate 80. The formulated bulk material contains approximately 3 to 7 g% (30 to 70 mg/mL) protein.

7. Warnings and Precautions

See [3](#) Serious Warnings and Precautions Box

General

Infusion Rate Precautions

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.

Transmission of 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.

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 health professional to have been transmitted by BAT to Emergent BioSolutions Canada Inc. at 1-800-768-2304 (phone) or medicalinformation@ebsi.com.

Monitoring and Laboratory Tests

Hypersensitivity

Monitor vital signs for signs and symptoms of acute allergic reactions 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.

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.

Sensitivity/Resistance

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. Medications such as epinephrine should be available for immediate 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.

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.

7.1. Special Populations

7.1.1. Pregnancy

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

7.1.2. Breastfeeding

It is unknown if Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine) is excreted in human milk. Precaution should be exercised because many drugs can be excreted in human milk.

7.1.3. Pediatrics

The effectiveness of BAT has not been established in pediatric patients; however limited pediatric safety data are available (see 8 Adverse Reactions).

7.1.4. Geriatrics

The safety, pharmacokinetics, and effectiveness of BAT have not been established in geriatric subjects (see 8 Adverse Reactions)

8. Adverse Reactions

8.1. Adverse Drug Reaction Overview

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 7 Warnings and Precautions)
- Delayed allergic reactions/serum sickness (see 7 Warnings and Precautions)
- Infusion reactions (see 7 Warnings and Precautions)

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies in the clinical trials of another drug.

The safety of BAT has been tested in healthy adults and patients with suspected botulism who were treated with BAT under an expanded access clinical study.

In two 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, 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%). 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 (age 10 days to 17 years; including 1 newborn, 3 infants and toddlers, 4 children and 7 adolescents) 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 were 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 (Table 4). 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.

The observed mortality rate was 11/228 (4.8%). None of these deaths were considered related to treatment with BAT.

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 serious adverse reaction of hemodynamic instability characterized by tachycardia, bradycardia and asystole during infusion of BAT.

Thirty-six geriatric subjects (>65 years of age) received BAT under the CDC expanded access clinical study. One geriatric subject experienced rash as an adverse reaction following infusion of BAT.

Table 4 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 |
| 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 |

| System Organ Class | Preferred Term | Overall (N=228) | | |
|---|----------------------------------|--------------------|--------------------|------------------|
| | | No. of Events | No. of Subjects | % of Subjects |
| 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.

8.3. Less Common Clinical Trial Adverse Reactions

Adverse reactions reported in less than 4% of healthy subjects in clinical trials included pyrexia and throat discomfort.

8.5. Post-Market Adverse Reactions

Hypersensitivity/allergic reactions have been reported in patients treated with BAT, including anaphylactic shock.

9. Drug Interactions

9.4. Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5. Drug-Food Interactions

Interactions with foods have not been established.

9.6. Drug-Herb Interactions

Interactions with herbs have not been established.

9.7. Drug-Laboratory Interactions

BAT contains maltose which can interfere with certain types of blood glucose monitoring systems. 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.

10. Clinical Pharmacology

10.1. Mechanism of Action

The mechanism of action of BAT is through passive immunization with equine polyclonal antibody fragments (primarily F(ab')₂ 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.

10.2. 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. The primary endpoint for the study was to evaluate the percent muscle function of the EDB muscle in both feet following exposure to Botulinum toxins Type A (BOTOX®) in the left foot and Type B (MYOBLOC®) in the right foot 24 hours after intravenous administration of Botulism Antitoxin Heptavalent (Equine) Types A-G or placebo. The percent muscle function is based on the preservation of the compound muscle action potential (CMAP) wave amplitude and area of the EDB muscle measured using a reference electrode. 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.

10.3. 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_{0-∞} and C_{max} 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 of Two vials of BAT

| Antitoxin Serotype | Treatment Group | AUC _{0-∞} (U*hr/mL) | C _{max} (U/mL) | t _{1/2} (hr) | Cl (mL/hr) | V _d (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 |
| 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_{max} = Maximum Serum Concentration; BAT = Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine); t_{1/2} = Half-life; T_{max} = Time to Maximum Serum Concentration; U = Unit; V_d = Volume of Distribution.

10.4. 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.

11. Storage, Stability and Disposal

Store frozen at or below -15°C until used.

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.

12. Special Handling Instructions

The product should be brought to room or body temperature immediately prior to use. The product should be clear or slightly opalescent. Do not use product that appears cloudy or contains particulates.

Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

| | |
|---|--|
| Non-Proprietary name of the drug substance: | Botulism Antitoxin Serotype A, B, C, D, E, F or G (Equine) |
| Chemical name: | Botulism Antitoxin Serotype A, B, C, D, E, F or G (Equine) |
| Molecular formula & molecular mass: | F(ab') ₂ of approximately 100 kDa and Fab approximately 50 kDa. |
| Structural formula: | Gamma immunoglobulin (IgG) polyclonal antibody fragments F(ab') ₂ and Fab. |
| Physicochemical properties: | Each BAT Drug Substance antitoxin serotype is a clear to opalescent, colorless to pale yellow liquid in an aqueous buffer (pH 5.0-6.5) containing equine derived antibody fragments that are targeted against one of the seven serotypes. The fragments are derived from digesting intact equine IgG monomers with the enzyme pepsin, resulting in F(ab') ₂ , Fab and F(ab') ₂ related fragments |

Product Characteristics:

BAT [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine)] is a sterile, clear to opalescent, colorless to pale yellow liquid containing enzymatically modified and purified equine derived gamma immunoglobulin (IgG) antibodies to the seven known botulinum toxin types (A-G).

BAT [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine)] is a sterile solution of F(ab')₂ and F(ab')₂-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 a 50 milliliter (mL) vial size. BAT is administered intravenously.

The manufacturing process for each antitoxin type includes cation-exchange chromatography to purify the immunoglobulin fraction, digestion with pepsin to produce F(ab')₂ and F(ab')₂-related immunoglobulin 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 6](#)).

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 virus filtration step which removes viruses based on size. The virus filtration step is therefore effective for all the above lipid-enveloped viruses as well as smaller non-enveloped viruses including equine rhinovirus, equine adenoviruses and adeno-associated viruses, and equine parvovirus.

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 (MIPLD₅₀) of botulinum neurotoxin for serotype A, B, C, D, F, and G and 1,000 MIPLD₅₀ of serotype E.

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

Viral Clearance

The two manufacturing steps were implemented specifically to reduce the risk of transmission of viral disease. The solvent/detergent 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 virus filtration step which removes viruses based on size. The virus filtration step is therefore effective for all the above lipid-enveloped viruses as well as smaller non-enveloped viruses including equine rhinovirus, equine adenoviruses and adeno-associated viruses, and equine parvovirus (see Table 6).

Table 6 Viral Clearance Capacity of the BAT Process

| | Enveloped | | | | | Non-enveloped | | |
|--|-----------|-------|-------|---------|---------------|---------------|-------|---------|
| First-generation Virus Filter | | | | | | | | |
| Genome | RNA | RNA | RNA | DNA | RNA | DNA | DNA | RNA |
| Virus | XMuLV | WNV | BVDV | PRV | PI3 | Ad2 | PPV | EMC |
| Family | Retro | Flavi | Flavi | Herpes | Paramyxo o | Adeno | Parvo | Picorna |
| Size (nm) | 80-110 | 40-70 | 50-70 | 150-200 | 100-200 | 70-100 | 18-24 | 25-30 |
| Virus filtration (log ₁₀) | ≥2.7 | ≥2.1 | ≥4.5 | n.t | n.t. | ≥4.7 | 4.5 | ≥4.5 |
| S/D (log ₁₀) | ≥4.3 | ≥5.1 | n.t. | ≥5.1 | ≥5.5 | n.t. | n.t. | n.t. |
| Total Reductio n (log ₁₀) | ≥7.0 | ≥7.2 | ≥ 4.5 | ≥5.1 | ≥5.5 | ≥4.7 | 4.5 | ≥4.5 |
| Second-generation Virus Filter | | | | | | | | |

| | | | | | | | | |
|---------------------------------------|-------------------|-------------------|------|-------------------|-------------------|------|-------------------|------|
| Virus Filtration (log ₁₀) | ≥4.3 ^a | ≥4.3 ^a | n.t. | ≥4.3 ^a | ≥4.3 ^a | ≥4.2 | ≥4.3 ^b | ≥5.0 |
| S/D (log ₁₀) | ≥4.3 | ≥5.1 | n.t. | ≥5.1 | ≥5.5 | n.t. | n.t. | n.t. |
| Total Reduction (log ₁₀) | ≥8.6 | ≥9.4 | n.t. | ≥9.4 | ≥9.8 | ≥4.2 | ≥4.3 ^b | ≥5.0 |

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

S/D: Solvent and detergent, n.t. – not tested

^aThe lowest parvovirus log reduction factor of ≥4.3 is applied based upon the mechanism of removal by size exclusion

^bThe PPV log₁₀ reduction factor was validated using worst-case or varying conditions for applied volume, protein concentrations, and filtration.

14. Clinical Trials

The effectiveness of BAT is based on efficacy studies demonstrating a survival benefit in animal models of botulism.

The safety has also been tested in two clinical trials in normal healthy human subjects BT-001 and BT-002 Stage B. These studies also examined the pharmacokinetics (PK) and pharmacodynamics (PD) of the BAT product (see 10 Clinical Pharmacology). A limited amount of safety information was also gathered from patients with suspected botulism who were treated with BAT under the CDC expanded access clinical study.

Animal Studies

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 two animal models: guinea pigs (Study #1) and Rhesus

macaques (Study #2).

Study Demographics and Trial Design

Table 7 Summary of Demographics for BAT Therapeutic Efficacy Studies in Animal Models

| Study # | Trial design | Species | Dosage, route of administration and duration | Number | Serotype | Animal Weight Range | BAT Antitoxin Dose |
|----------|--|----------------------|--|---|----------|---------------------|----------------------|
| Study #1 | Pivotal, randomized, blinded, placebo controlled GLP study | Guinea Pig (Hartley) | Single IV dose of BAT or placebo following toxin challenge (1.5xGPIMLD ₅₀) and observation of fourth consecutive moderate/severe clinical sign | N=476 34 = Placebo (17 per sex per serotype) 34 = BAT (17 per sex per serotype) | A to G | 400-500 g | 1x scaled human dose |
| Study #2 | Pivotal, randomized, blinded, placebo controlled GLP study | Rhesus Macaque | Single IV dose of BAT or placebo following toxin challenge (1.7xNHPLD ₅₀) and observation of onset of moderate/severe clinical sign | N=60 30 = Placebo (15/sex) 30 = BAT (14 males and 16 females) | A | 3.28 – 7.0 kg | 1x scaled human dose |

BAT = Botulism Antitoxin Heptavalent; IV = Intravenous; GPIMLD₅₀ = Guinea Pig Intramuscular Lethal Dose 50%; NHPLD₅₀ = Non-human Primate Lethal Dose 50%

In the first pivotal study (Study #1), guinea pigs were intoxicated with one of the seven botulinum neurotoxin (BoNT) serotypes (A-G) at a dose equivalent to 1.5x guinea pig intramuscular lethal dose 50% (GPIMLD₅₀), which would be expected to cause death in the majority of untreated animals.

The toxin was administered via intramuscular injection into the right hind limb. At the onset of four consecutive moderate or severe clinical signs (right hind limb weakness, salivation, lacrimation, weak limbs and noticeable changes in breathing rate or pattern), groups of thirty four animals per serotype were treated with either placebo control or 1x scaled human dose of BAT (weight/weight based on an average human body weight of 70 kilograms), intravenously and observed for twenty one days. The objective of the study was to determine any statistically significant enhancement in survival of BAT treated animals, when compared to placebo controls.

In the second pivotal study (Study #2), Rhesus macaque were intoxicated intravenously with

BoNT serotype A dose equivalent to 1.7x non-human primate lethal dose 50% (NHPLD₅₀/kg) and administered either 1x scaled human dose of BAT (n=30) or placebo control (n=30) intravenously at the onset of clinical signs (ptosis, muscular weakness, or respiratory distress). Following treatment all animals were provided supportive care (nutritional) and observed for 21 days. The objective of this study was to confirm the therapeutic effect of a single intravenous dose of BAT when administered at the onset of clinical signs and in combination with minimal (nutritional) supportive care, in preventing mortality in BAT treated animals when compared to placebo controls.

Study Results

Guinea Pig Model, Primary Efficacy (Survival)

Table 8 Summary of Guinea Pig Survival Data

| 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%) | |
| 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).

Treatment with a single dose of (1x scaled human dose) BAT administered to symptomatic animals resulted in a statistically significant enhancement in survival over placebo control animals, irrespective of the intoxicating serotype.

Nonhuman Primate (Rhesus macaque), Primary Efficacy (Survival)

Table 9 Survival Results of Study #2 and Statistical Significance

| Treatment | Survival (%) | Fisher's Exact Test (p-value) |
|-----------|--------------|-------------------------------|
|-----------|--------------|-------------------------------|

| | | |
|-----------------|-------------|-----------|
| 1x BAT | 14/30 (47%) | p< 0.0001 |
| Placebo Control | 0/30 (0%) | |

LBERI = Lovelace Biomedical and Environmental Research Institute; BAT = Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) – (Equine).

Treatment with BAT resulted in a statistically significant improvement in survival when compared to placebo controls (Table 9). None of the Rhesus macaques challenged with botulinum neurotoxin serotype A complex and treated with placebo survived to the end of the study, whereas 14 of 30 (46.7%) nonhuman primates treated with BAT survived to the end of the study.

This difference in survival rates between the two groups was statistically significant (p<0.0001) using the Fisher's exact test (Table 9).

14.1. Clinical Trials by Indication

14.1.1. 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

In a randomized, single-center, double-blind trial the pharmacokinetics and safety of BAT was evaluated in 40 healthy subjects ranging in age between 19 to 52 years of age 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). A brief summary of the results can be found in Part 1: Clinical Pharmacology, Pharmacokinetics.

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. A brief summary of the results can be found in Part 1: Clinical Pharmacology, Pharmacodynamics.

Table 10 Summary of Subject Demographics for BAT Clinical Trials

| Study # | Trial Design | Dosage, Route of Administration and Duration | Study Subjects (n = number) | Age Range | Gender |
|---------|---|---|---|---------------|------------------|
| BT-001 | Phase 1, single center, randomized, double blind parallel armed safety and PK study in normal healthy subjects. | Single IV dose (1 vial) or double IV doses (2 vials) of BAT (Single administration) | N=40 20 = (1 vial) 20 = (2 vials) | (19-52 years) | M = 20 F = 20 |

| Study # | Trial Design | Dosage, Route of Administration and Duration | Study Subjects (n = number) | Age Range | Gender |
|-----------------------------|---|---|---|----------------------------|-------------------|
| BT-002 Stage B | Phase 1a/2b, single center, randomized double blind, parallel arm safety and PD study following IV administration of either BAT or placebo to normal healthy subjects administered BoNT serotypes A or B in the EDB muscle. | Single IV dose (one vial) of BAT or Placebo | N=26 10 = Placebo 16 = BAT (1 vial) | (19-48 years) | M = 13 F = 13 |
| CDC expanded access program | Open label, observational expanded access clinical study for the treatment of subjects with suspected or confirmed botulism. | Single IV dose = (1 vial=143 patients) Double IV doses = (2 vials= 5 patients) | N=148 | 46 years (10 days-88years) | M = 105 F = 43 |

BAT = Botulism Antitoxin Heptavalent; BoNT = Botulinum Neurotoxin; BAT AB = Antitoxin Bivalent (Equine) Types A and B (Aventis Pasteur); EDB = Extensor Digitorum Brevis; IV = Intravenous; PD = Pharmacodynamics; PK = Pharmacokinetics; CDC = Centers for Disease Control and Prevention

To provide additional support for the efficacy demonstrated in the animal models, a preliminary analysis of data from the CDC open-label, observational expanded access clinical study for the treatment of subjects with suspected or confirmed botulism with BAT was conducted. The purpose of the CDC expanded access program was to enable the use of the investigational BAT product for treatment of individuals with botulism in the United States, as a result of naturally occurring outbreaks or in cases of isolated, unintentional incidents. 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). The rationale behind this analysis was that early treatment with BAT would prevent symptom progression and reduce disease duration; however, later treatment would be less effective since BAT does not have an effect on BoNT once it has acted upon the cholinergic nerve endings.

Study Results from the CDC Open-label, Observational Expanded Access Clinical Study

Table 11 Summary of Duration of Hospitalization, ICU Stay and Mechanical Ventilation for CDC Patients Treated with BAT

| | Time from Symptoms to Treatment | Number of Patients (N) | Mean Duration in Days (SD) |
|-----------------|---------------------------------|------------------------|----------------------------|
| Hospitalization | ≤ 2 Days | 14 | 12.4 (9.28) |
| | > 2 Days | 72 | 26.1 (26.37) |

| | | | |
|------------------------|----------|----|--------------|
| ICU Stay | ≤ 2 Days | 13 | 9.2 (7.40) |
| | > 2 Days | 70 | 15.8 (18.76) |
| Mechanical Ventilation | ≤ 2 Days | 9 | 11.6 (7.83) |
| | > 2 Days | 41 | 23.4 (21.11) |

In order to determine if BAT was efficacious in treating patients with botulism, duration of hospitalization was selected as the primary end point. A post-hoc statistical analysis of the CDC patient information to determine if treating patients early after symptom onset (≤ 2 days) versus later (> 2 days) had an effect on the duration of hospitalization. Overall, the mean duration of hospitalization for patients with botulism was 23.2 days. If patients were treated with BAT within 2 days of symptom onset, the duration of hospitalization was 12.4 ± 9.28 days but if the patients were treated more than 2 days after symptom onset, the duration of hospitalization was 26.1 ± 26.37 days (Table 11). This suggests that early treatment (≤ 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 11) and is consistent with the mechanism of action (see Part 1: Clinical Pharmacology, Mechanism of Action).

15. Microbiology

No microbiological information is required for this drug product.

16. Non – Clinical Toxicology

No toxicity studies have been performed to evaluate the toxicity potential of BAT.

Results from the PK/PD studies performed in guinea pigs and rhesus macaques in support of efficacy did not reveal any toxicity concerns, when tested up to 5x scaled human dose.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

BAT[®]

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

“HEALTH CANADA HAS AUTHORIZED THE SALE OF THIS EXTRAORDINARY USE NEW DRUG FOR DOCUMENTED OR SUSPECTED EXPOSURE TO BOTULINUM NEUROTOXIN SEROTYPES A, B, C, D, E, F AND G BASED ON LIMITED CLINICAL TESTING IN HUMANS”

This Patient Medication Information is written for the person who will be taking **BAT**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **BAT**, talk to a health care professional.

Serious Warnings and Precautions

- Prepare for monitoring and management of hypersensitivity reactions, infusion reactions or delayed allergic reactions (serum sickness)
- BAT is prepared using pools of equine plasma, therefore may carry the risk of transmitting infectious agents (see Transmission of Infectious Agents section)

What BAT is used for:

- BAT is a botulism antitoxin made from the plasma of horses which may make the illness from botulism less severe.
- Botulism is a muscle-paralyzing disease caused by the toxin made by a bacterium called *Clostridium botulinum* which can cause the following conditions: double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, muscle weakness that spreads through the body and difficulty breathing. BAT can also cause paralysis and death.
- Treatment with BAT will not reverse the paralysis but may decrease the duration and extent of paralysis.

How BAT works:

BAT contains antibody fragments which can neutralize botulism toxins. 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.

The ingredients in BAT are:

Medicinal ingredient(s): antitoxins to serotypes A to G.

Non-medicinal ingredient(s): maltose, polysorbate 80

BAT comes in the following dosage form(s):

BAT is a sterile solution for intravenous injection provided in a single use 50 mL glass vial. Each vial contains a minimum potency of >4500 U serotype A antitoxin, >3300 U serotype B antitoxin, >3000 U serotype C antitoxin, >600 U serotype D antitoxin, >5100 U serotype E antitoxin, and >3000 U serotype F antitoxin, and >600 U serotype G antitoxin as listed in 6 Dosage Forms, Strengths, Composition, and Packaging.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take BAT. Talk about any health conditions or problems you may have, including if you:

- You have experienced allergic reactions to horses, horse blood products, asthma or hay fever in the past.
- Are pregnant or nursing.

Other warnings you should know about:

- BAT is made from horse plasma and therefore may contain infectious agents such as viruses that can cause disease. This risk has been reduced by screening the horses for certain viruses and by inactivating or removing viruses during the manufacturing process.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with BAT:

- Drugs that may interact with BAT have not been established.
- BAT contains maltose that can interfere with certain types of blood glucose monitoring systems (tests that check the level of sugar in your body).

How to take BAT:

BAT will be administered by a healthcare professional by an injection into your vein.

Usual dose:

Your doctor will determine the dose of BAT. The treatment may take several hours to administer.

Possible side effects from using BAT:

The most common side effects of BAT are headaches, fever, rash, hives, chills, nausea and 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.

Tell your healthcare professional 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 healthcare professional 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.

These are not all the possible side effects you may have when taking BAT. If you experience any side effects not listed here, tell your healthcare professional.

Serious side effects and what to do about them

| Frequency/Side Effect/Symptom | Talk to your healthcare professional | | Stop taking this drug and get immediate medical help |
|--|--------------------------------------|--------------|--|
| | Only if severe | In all cases | |
| UNCOMMON | | | |
| Hemodynamic Instability | | √ | √ |
| Serum Sickness | | √ | √ |
| Anaphylaxis | | √ | √ |
| Allergic Reaction (trouble breathing, swollen tongue or lips, fast heart rate) | | √ | √ |

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or;
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store frozen at or below -15°C until used. Do not refreeze.

Keep out of reach and sight of children.

If you want more information about BAT:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada Drug Product Database website (Drug Product Database: Access the database); the manufacturer's website (www.emergentbiosolutions.com); via email at medicalinformation@ebsi.com, or by calling 1-800-768-2304

This leaflet was prepared by Emergent BioSolutions Canada Inc.

Date of Authorization: [YYYY-MM-DD]

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