

All Designated Holding Centres

7 December 2016

Dear Colleague,

Supply of Botulism antitoxin

According to our records, you are currently holding doses of Botulism Anti-Toxin (BAT) manufactured by Novartis Vaccines, and supplied to you by Public Health England (PHE).

Further to our previous letter of 14 November 2016, PHE will start to distribute Emergent Biosolutions BAT alongside Novartis Vaccines BAT to replace any Novartis product which is used or expires whilst you are holding it in stock.

There are several key differences between the Emergent Biosolutions and Novartis products which are described below and in detail at Annex A.

The Emergent Biosolutions BAT:

- is a heptavalent product which contains neutralising antibodies for 7 botulinum toxins, types A, B, C, D, E, F and G;
- is presented in a 20mL vial (see fill volume on the carton label) which must be diluted 1 in 10 with Sodium Chloride 0.9% Infusion before administration;
- is indicated as a single dose (i.e. you will be sent 1 vial rather than 3 bottles as previously);
- has separate dosage instructions for adults, children and infants (under 1 years old);

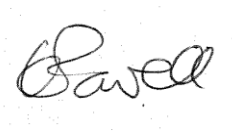
- **should be stored between 2°C and 8°C.** However, please note that the storage conditions in the product information and on the vial label indicates that the antitoxin should be stored in a freezer at <-15°C. **The UK stock has been thawed and should continue to be stored between 2°C and 8°C.** **The product must not be re-frozen.**
- has been re-packed by Movianto UK for PHE into packs of one 20mL vial and one product information leaflet.

Further detailed guidance on preparation and administration of the product is provided in the product information leaflet which will be contained within the BAT re-packed box, and can also be found at Annex B.

Holding centres should ensure they retain their existing stocks of Novartis BAT for use on a named-patient basis up until expiry at which point it will be replaced with the Emergent Biosolutions BAT.

If you have any queries about the above, please email vaccinesupply@phe.gov.uk

Yours sincerely



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Annex A

Table comparing the Novartis and new Emergent Biosolutions Botulism Antitoxins

Supplier	Novartis Vaccines	Emergent Biosolutions
Product Name	Botulism Antitoxin Behring	BAT - Botulism Antitoxin Heptavalent (A,B,C,D,E,F,G) – (Equine)
Botulinum neurotoxin serotype antitoxins	Trivalent – Serotypes A,B and E	Heptavalent – Serotypes A,B,C,D,E,F and G
Source of immune sera	Equine	Equine
Presentation	250 ml infusion bottle – ready to use	20 mL vial – Contents should be diluted 1:10 in 0.9% sodium chloride injection. The contents of the entire vial (as the fill volume of the vial varies per batch) should be drawn-up into a syringe to measure the volume of liquid in the vial and a volume of sodium chloride 0.9% should then be calculated and added to achieve the 1 in 10 dilution.
Dosage	2 x 250ml vials initially with the option of a further 250ml depending on clinical progress. Adults and children are given the same dose	1 vial for adults 17 years and older. Dosage adjustment based on body weight for children over 1 year of age. Infants under 1 are given 10% of the adult regardless of body weight. (See example below this table for further information). Advice in the product information on infusion rates should be followed. Single dose only –no additional doses recommend in the company leaflet.
License Status	Unlicensed in UK – German Marketing Authorisation	Unlicensed in UK – Approved by the FDA in the US
Storage	Store in a refrigerator between 2 and 8°C.	Store in a refrigerator between 2 and 8°C. Note however, that the storage conditions in the product information and on the vial label indicates that the antitoxin is stored in a freezer. <u>The UK stock has been thawed and should continue to be stored in a refrigerator at 2-8°C. The product must not be re-frozen.</u>
Adverse events	Risks of adverse events including hypersensitivity and anaphylaxis. Treatment advice is given in the product information leaflet.	Risks of adverse events including hypersensitivity and anaphylaxis. Full list given in the product information leaflet. Treatment advice for adverse events is given in the product information leaflet and the Green Book chapter ‘Vaccine safety and the management of adverse events following immunisation’.
Other information		Product has been re- packed for PHE by Movianto UK.

Paediatric Dosing:

For the new heptavalent Emergent Biosolutions BAT product, EQUINE, please note that there is a difference in the dosing and administration for children compared to adults. The administration guidance in the product insert states,

'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 millilitres per vial), 90 to 200 millilitres 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 paediatric dosing), the entire content of the vial should be withdrawn to ensure accurate calculation of the dosage [Table 2].'

Although the presentation of BAT is usually 20ml vials, please make sure to check the fill volume of each vial you have in stock at point of dilution, as the fill volume may differ from batch to batch as stated in the product insert.

To help clarify any ambiguities,

For paediatric dosing, a worked example is shown below:

Patient weight – 40kg, Age 12 years

For vial batch number 0487, fill volume = 18ml

Dilute 1 in 10 for vial batch number 0487

i.e. Add 18ml, (contents of the WHOLE vial) to 162ml of Sodium chloride injection 0.9%

From table 2 of the product insert, child weighing 40 - 44kg requires 70% of adult dose.

$70/100 \times 180\text{ml} = 126\text{ml}$ (this is the volume required for this child).

See table 1 of product insert for corresponding infusion rate for child age 1 – 17 years.

Annex B

Emergent Biosolutions Botulism Antitoxin Product Information Leaflet

See attachment in email