

## **HPA recommendation on the treatment and prophylaxis of tetanus**

### **Background**

During the recent shortage in the supply of tetanus immunoglobulin (TIG) the supply of TIG has been restricted to patients requiring treatment for suspected tetanus. Individuals with tetanus prone wounds have been unable to receive TIG prophylaxis and have had to rely on tetanus boosters and antibiotics at the time of injury. In addition, the supply of TIG limited for treatment was in an intramuscular format and therefore, the volume required (around 30mls) could not be given without causing major discomfort.

After discussions with BPL, it became apparent that normal preparations of immunoglobulin (for IV and sub-cutaneous use) contained reasonable levels of tetanus antibody when measured by ELISA. In 2008, we therefore arranged for batches of two products Subgam (Human normal immunoglobulin solution 160g/L - the human normal immunoglobulin preparation suitable for IM or SC use) and Vigam (5 g% normal immunoglobulin – the human normal immunoglobulin preparation suitable for IV use) to be measured for levels of tetanus antibodies by ELISA and in vivo to determine if it would be a suitable alternative should the current stock shortage continue. Further ELISA testing has been performed on batches of Subgam, Vigam and Gammplex (a new IV immunoglobulin product) in 2011. In addition, in 2011 ELISA testing has also been undertaken on Gammplex (5 % w/v normal immunoglobulin) another human normal immunoglobulin preparation produced by BPL suitable for IV use.

### **Results**

The testing was performed at the National Institute for Biological Standards and Control revealed a good correlation between ELISA and in vivo Toxin Neutralising Test (TNT) anti-toxin assays for both Vigam and Subgam (table). The following levels can be used to estimate the equivalent doses of normal immunoglobulin to achieve the recommended dose of tetanus anti-toxin:

### **Recommendation**

The HPA therefore recommends that if hospitals can source suitable stocks of tetanus specific immunoglobulin this should be used for the treatment of tetanus cases and the prophylaxis of tetanus prone wounds.

Where suitable TIG stock cannot be sourced, the HPA recommends that human normal immunoglobulin for intravenous use (Vigam) may be used as an alternative for treatment of clinical tetanus. The volume of Vigam required to achieve the recommended treatment dose of 5,000-10,000 iu will be approximately 250 to 500mls. This can be infused over a period of 3-6 hours. For tetanus prone wounds requiring TIG, human normal immunoglobulin for subcutaneous use (Subgam) may be given intramuscularly as an alternative if stocks of TIG are not available. The volume of Subgam required to achieve the equivalent of the recommended dose of 250iu of tetanus anti-toxin will be approximately 5mls – equivalent to one vial of 750mg.

Trusts should contact BPL as appropriate for the supply (020 8258 2342).

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**Table: Results from Tetanus Antitoxin assays for Human Normal Immunoglobulin**

<b>Year of testing</b>	<b>Batch number</b>	<b>Product</b>	<b>ELISA iu/ml</b>	<b>TNT assay iu/ml</b>
2008	SCBN7647	Subgam	63	57 (48-69)
2008	SCBN7651	Subgam	64	57 (48-69)
2011	SCBN8611	Subgam (750mg)	66.4	
2011	SCBN8949	Subgam (750mg)	56.9	
2011	SCAN9129	Subgam (1500mg)	60.8	
<b>Year of testing</b>	<b>Batch number</b>	<b>Product</b>	<b>ELISA iu/ml</b>	<b>TNT assay iu/ml</b>
2008	VLAN7724	Vigam	23	26 (18-46)
2008	VLAN7759	Vigam	20	18 (15-22)
2008	VLAN7730	Vigam	23	21 (18-26)
2011	VLCN9116	Vigam (5g)	17.5	
2011	VLCN9117	Vigam (5g)	17.9	
2011	VLAN9219	Vigam (10g)	15.9	
2011	VLAN9220	Vigam (10g)	15.9	
<b>Year of testing</b>	<b>Batch number</b>	<b>Product</b>	<b>ELISA iu/ml</b>	<b>TNT assay iu/ml</b>
2011	VSCN8627	Gammaflex (5g)	17.8	
2011	VSCN9016	Gammaflex (5g)	17.2	
2011	VSCN9156	Gammaflex (5g)	19.6	
2011	VSAN8599	Gammaflex (10g)	21.6	
2011	VSAN9070	Gammaflex (10g)	16.7	
2011	VSAN9083	Gammaflex (10g)	17.6	

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