21 December 2010

BIOSTATE® Advisory Statement

CSL Biotherapies has recently received reports of two patients with von Willebrand disease (VWD) being under-dosed with BIOSTATE due to a misunderstanding regarding the prescribing haematologist's dosing instructions. In both cases the patient outcome was advised as satisfactory. However to limit the possibility of a similar future episode, CSL Biotherapies, the Australian Haemophilia Centre Directors Organisation (AHCDO), the Australian Haemophilia Nurses Group (AHNG), and the Australian Red Cross Blood Service (the Blood Service) have jointly prepared this statement and recommendation.

BIOSTATE contains two active entities - factor VIII (FVIII) and von Willebrand factor (VWF), in a 1:2 ratio. BIOSTATE is approved by the TGA for use in both haemophilia A (HA) and von Willebrand disease (VWD).

Upon receipt of TGA approval of BIOSTATE for the treatment of bleeding episodes in VWD (27 Aug 2008), CSL Biotherapies amended the BIOSTATE carton and vial to clearly state the content of both active entities (FVIII and VWF). This change was made to comply with the TGA's *Therapeutic Goods Order No. 69 - General requirements for labels and medicines* (*TGO 69*) which requires that the name(s) and quantity of all active ingredients contained in a prescription medicine should be displayed on the main label of the carton and *Best Practice Guidelines on Prescription Medicine Labelling (Nov 2005)* which states that the name(s) and strength(s) of the active ingredient(s) contained in a prescription medicine should be prominently and equally displayed on the carton.

Background to the two reports

Each involved a VWD patient presenting out of hours :-

In the first case the duty haematologist instructed '2,500 units of BIOSTATE'.
Staff administered BIOSTATE - 2,500 IU of VWF (ie 1,250 IU of FVIII), whereas the haematologist had intended BIOSTATE - 2,500 IU of FVIII.

In the second case the duty haematologist instructed '8,000 units of BIOSTATE'.
Staff administered BIOSTATE - 8,000 IU of VWF (ie 4,000 IU of FVIII), whereas the haematologist had intended BIOSTATE - 8,000 IU of FVIII.

Recommendation

CSL Biotherapies has discussed these two cases with AHCDO, the AHNG, and the Blood Service, and all parties have agreed on the on the following recommendation :-

That all centres that stock or administer BIOSTATE should consider amending :

- Clinical Practice Guidelines used by haematologists and in haemophilia treatment centres, and
- Dispensing protocols for BIOSTATE used in Blood Banks and/or Pharmacies

such that both documents clearly state the following information :

- BIOSTATE contains both FVIII and VWF in a 1:2 ratio, and is approved for use in both haemophilia A and von Willebrand disease
- Each order for BIOSTATE should specify the 'active entity' of the ordered dose :-
  examples :- "BIOSTATE - 1000 IU of VWF"
  "BIOSTATE - 1500 IU of FVIII"
- Any order for BIOSTATE that does not specify the 'active entity' of the ordered dose should be clarified before the order is processed.

Please do not hesitate to contact any of the following people regarding this statement :-

Dr Chris Fry	Dr Chris Barnes	Mr Stephen Matthews	Dr Joanne Pink
Senior Product Manager	Chair	Co-chair	Chief Medical Officer
CSL Biotherapies	Australian Haemophilia Centre	Australian Haemophilia	Australian Red Cross
ph 03 9246 5723	Directors' Organisation	Nurses' Group	Blood Service

BIOSTATE presentations

	WFI	Final Concentration (1)		Colour wedge on carton and label		
TGA approved and currently supplied:-	volume	FVIII	VWF	current	future (2)	Item No
BIOSTATE 250 IU FVIII / 500 IU VWF	5mL	50 IU/mL	100 IU/mL			33000185
BIOSTATE 500 IU FVIII / 1,000 IU VWF	10mL	50 IU/mL	100 IU/mL			33000192
TGA approved and not yet supplied :-						
BIOSTATE 1,000 IU FVIII / 2,000 IU VWF(3)	10mL	100 IU/mL	200 IU/mL			n/a

(1) nominal
(2) the colour wedge on BIOSTATE 250IU FVIII / 500 IU VWF will be changed to assist visual differentiation. Advice will be circulated at the time of change.
(3) TGA approval 5 Feb 2009 - supply awaiting outcome of NBA Schedule 4 funding submission.