



## Review of octaplex® utilization in Canada Fall 2010 Audit Summary Report

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To further follow up on the dosing, indication and INR correction survey data received from the original octaplex® audit, the National Advisory Committee coordinated a broader scale audit that was performed in the fall of 2010. The original survey had been sent to the 20 institutions who had received the largest stock of the prothrombin complex concentrate product from CBS. The follow-up survey was sent to 201 institutions who receive octaplex® from Canadian Blood Services. A total of 111 facilities responded (55%). Of those, only 63 facilities infused octaplex® during the time period in question. A total of 134 patients received the product, nine of which received more than one dose.

Summary data for dosing, INR correction and clinical indications are provided in Tables 1 through 7. Although there may be inherent errors in this data due to the mechanism by which it was collected (survey data which may not have been completed by the attending / ordering physician), it has been used to aid in the revision of the National Advisory Committee's dosing recommendation for prothrombin complex concentrates. The dosing recommendation will change from the standard dose of 1000 IU (or 40 mL) to 1000 IU if INR <3.0; 2000 IU if INR 3.0-5.0 and 3000 IU if INR >5.0. Although there were several cases (41%) in which Vitamin K antagonism / deficiency was not clearly documented and rare indications (5%) in which the 2008 recommendations for patients on Vitamin K antagonists were not followed, there will be no change made to the original Indicated for / Contra-indicated in / Not recommended list by the Prothrombin Complex Working Group in the revised recommendations. The data also identified a number of patients who did not appear to receive concurrent Vitamin K (40%) and/or post dose monitoring of INR (15%) which are recommended to ensure sustained and efficient reversal of the vitamin K antagonist. This may highlight an area of ongoing educational need.

Review of adverse outcomes submitted by participating institutions was limited by the fact that 29 and 41 out of the 134 patients did not have available data for 30 day mortality or thrombosis, respectively. A reported 31 out of the 134 patients (23%) died



within 30 days post octaplex®, but no deaths were directly attributed to PCC therapy. A total of five thromboembolic complications were reported -1 pulmonary embolus- PE, 1 cerebrovascular infarct –CVA and 3 had no further classification provided. Two patients received a 1000 IU dose, two patients (PE and CVA) received a 2000 IU dose and one patient received a 3000 IU dose. Three of the five patients with documented thrombotic complications received the product for line or catheter insertion.

Table 1: Dose of PCC and INR correction -all

Dose of PCC	Number of patients	Vitamin K administration documented	Pre INR range (n)	Post INR range (n)	% correction to 1.5 or less	
					Actual	Worst case*
500 IU	5	0	1.6-3.5 (4)	1.3 (2)	100	50
1000 IU	70	49	1.4-17.0 (70)	1.1-3.3 (58)	50	41
1500 IU	13	2	1.9-8.6 (13)	1.2-1.5 (11)	100	85
2000 IU	30	22	1.7->13.0 (30)	1.1-2.3 (28)	64	60
2500 IU	2	1	3.5-4.7 (2)	1.6 (2)	0	0
3000 IU	10	5	2.1->25.0 (10)	1.1-1.9 (10)	80	80
> 3000 IU	4	2	2.1->10.0 (4)	0.9-1.5 (4)	100	100

\*worst case = percentage correction calculation using all non available post infusion INRs as if they were >1.5

- Secondary analysis was performed excluding all data from patients with no clear history of vitamin K antagonism and secondary doses with no significant difference in the dose correction results.



Table 2: Dose of PCC and INR correction for patients with Pre-octaplex INR values >5.0

Dose of PCC	Number of patients	Vitamin K administration documented	Pre INR range	Post INR range (n)	% correction to 1.5 or less	
					Actual	Worst* case
1000 IU	15	12	5.21-17.0	1.5-3.2 (14)	14	13
1500 IU	1	0	8.6	1.5 (1)	100	100
2000 IU	9	8	5.22- >13.0	1.2-2.3 (9)	55	55
3000 IU	3	1	5.1->25.0	1.1-1.5 (3)	100	100
> 3000 IU	2	1	5.16- >10.0	0.9-1.5 (2)	100	100

\*worst case = percentage correction calculation using all non available post infusion INRs as if they were >1.5.

Table 3: Dose of PCC and INR correction for patients with Pre-octaplex INR= 3.0-5.0

Dose of PCC	Number of patients	Vitamin K administration documented	Pre INR range	Post INR range (n)	% correction to 1.5 or less	
					Actual	Worst* case*
500 IU	1	0	3.5	N/A	N/A	0
1000 IU	14	10	3.0-4.6	1.3-2.4 (11)	50	39
1500 IU	4	1	3.0-4.4	1.2-1.5 (3)	100	75
2000 IU	11	6	3.1-4.9	1.1-1.9 (10)	70	64
2500 IU	3	1	3.5-4.7	1.2-1.6 (3)	33	33
3000 IU	5	3	3.1-4.7	1.1-1.9 (3)	60	60

\*worst case = percentage correction calculation using all non available post infusion INRs as if they were >1.5.



Table 4: Dose of PCC and INR correction for patients with Pre-octaplex INR values <3.0

Dose of PCC	Number of patients	Vitamin K administration documented	Pre INR range	Post INR range (n)	% correction to 1.5 or less	
					Actual	Worst case*
500 IU	4	0	1.6-1.88	1.3 (2)	100	50
1000 IU	41	27	1.4-2.99	1.1-1.8 (32)	72	56
1500 IU	8	2	1.9-2.4	1.2-1.5 (8)	100	100
2000 IU	10	6	1.7-2.9	1.2-1.7 (9)	89	80
2500 IU	0	N/A				
3000 IU	1	1	2.1	1.4	100	100

\*worst case = percentage correction calculation using all non available post infusion INRs as if they were >1.5

Table 5: Clinical Indication by Dose

		Dose of octaplex® received							Total
		500	1000	1500	2000	2500	3000	>3000	
Warfarin - Yes	Intracranial hemorrhage	1	12	1	2	0	1	0	17
	Major Bleeding <sup>1</sup>	1	15	2	7	1	2	1	29
	Urgent Procedure <sup>2</sup>	0	11	0	9	1	4	1	26
	Elective Procedure or Minor Bleeding <sup>4</sup>	0	5	0	1	0	0	1	7
Warfarin – No / Not indicated	Gastrointestinal Bleed <sup>4</sup>	0	7	2	4	0	0	0	13
	Other <sup>3</sup>	3	20	8	7	0	3	1	42
<b>Total</b>									<b>134</b>

<sup>1</sup> Bleeding documented as slowed or stopped in 18 cases, as no effect in 1 case and no available information in the remaining 10 cases.

<sup>2</sup> Eight of the urgent procedures included line or drain insertions.

<sup>3</sup> See Table 6 for list of clinical indications in other -warfarin -no / not indicated.

<sup>4</sup> Subset evaluation of the Elective procedures and Gastrointestinal bleeds was performed. Elective procedures had a Pre-INR range of 1.6-3.8 with an “actual” correction rate of



80% whereas the Gastrointestinal bleed patients had a much wider Pre-INR range of 1.9-17.0 with an actual correction of 73%.



Table 6. Indications in Other -Warfarin – No/ Not indicated.

<b>Other – Indication provided</b>
Adult dose
Below knee amputation
Factor II deficiency
Active bleed – trachea
SDH31/
Laparotomy
Thoracentesis
Heart transplant
Heart transplant
AA
MS
Shunt pre-dialysis
Post bronch to OR
Pre-CVC line for dialysis
Pre-CVC line for dialysis
Broken Nose
Chart not available
Major Bleeding
Major Bleeding
Laparotomy for bowel obstruction
Subdural hematoma
Bowel obstruction
Wound dehiscence
Urgent surgery
Atrial fibrillation
Scope for GI bleed
Head injury
Abscess drainage
Head injury
Chest tube insertion
AAA
SDH
Hernia repair
Epistaxis
IAB insertion
LCVA-ISH
ICH craniotomy
Heart transplant
Sternal rewire
Sepsis – central line
Laparoscopy
Dr. required