Appendix B: Reported risk of thromboembolic events associated with anticoagulation reversal agents used in non-transplant patients						
Author	Study Type; Number of patients	Product	Study population	TE Events	Follow up	Relevant major exclusions
Sarode et al (29)	Prospective RCT, open-label; N=216 (adverse events data reported in 212 patients)	4F-PCC (n=103) Vs Plasma (n=109)	Non-surgical adults with INR ≥2.0	7.8% (4F-PCC) 6.4 (Plasma)	Events recorded up to 10 days (visit window days 7-11); severe AE's screened for up to 45 days (visit window days 43-51)	• Those receiving non-study blood products prior to 4F-PCC administration except for PRBCs
Goldstein et al (7)	Prospective RCT, open-label; N=181 (adverse events data reported in 176 patients)	4F-PCC (n=88) Vs Plasma (n=88)	Urgent surgical or invasive procedure with INR ≥2.0	7% (4F-PCC) 8% (Plasma)	Events recorded up to day 10 (visit window days 7–11) and serious adverse events up to day 45 (visit window days 43–51).	• Patients receiving vitamin K prior to surgery (3 hours for intravenous and 6 hours for oral) • Those receiving non-study blood products prior to 4F-PCC administration except for PRBCs
Steiner et al (30)	Prospective RCT, open-label; N=50	4F-PCC (n=27) Vs Plasma (n=23)	VKA associated intra-cranial hemorrhage	25.9% (4F-PCC) 8.7% (Plasma)	Events recorded up to 90 days	• NYHA III/IV CHF, use of antiplatelets within 24 hours
Kushimoto et al (19)	Prospective RCT, open-label; N=11	4F-PCC	6 patients with acute bleeding and 5 with surgical bleeding	18% overall; 40% (n=2) of the surgical group	Events recorded to day 14 (visit window 12-16); severe AE reported to day 45 (visit window 43-47)	• Those receiving non-study blood products prior to 4F-PCC administration except for PRBCs
Bruckner et al (17)	Retrospective; N=62	rFVIIa	LVAD patients with bleeding	22.6% overall	Events recorded up to 7 days following administration	
Levi et al (31)	• Review of clinical using rFVIIa • 35 RCTs (26 involving patients and 9 involving healthy volunteers; N=4468 subjects (n=4119 patients and n=349 healthy volunteers), prevalence of TE events was 9.0%. Risk of arterial TE events was higher with rFVIIa compared to placebo (5.5% vs. 3.2%, P=0.003). Risk of venous TE events was similar between rFVIIa and placebo (5.3% vs. 5.7%). • Risk of arterial TE events was higher among those receiving rFVIIa and ≥65 years of age compared to placebo (9.0% vs. 3.8%, P=0.003)					