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Scottish Trauma Network Interim Policy Statement: Apixaban and rivaroxaban reversal with andexanet alfa in traumatic major haemorrhage

This statement consists of expert opinion from those within the Scottish Trauma Network (STN) including haematology, critical care and emergency medicine, using currently available evidence.

Summary

The STN does not recommend the *routine* use of andexanet alfa in those patients on apixaban or rivaroxaban with life-threatening traumatic major haemorrhage. In cases where definitive haemorrhage control is not an option or unsuccessful, andexanet alfa could be considered as a therapeutic option, following multidisciplinary discussion, when death from exsanguination is a likely outcome.

Context

Concerns have been raised regarding the safety profile of andexanet alfa in reversing the effects of apixaban and rivaroxaban in those sustaining traumatic major haemorrhage. In several recent cases, patients have suffered either serious complications or died as a result of widespread thrombotic events following traumatic major haemorrhage management that has included the use of andexanet alfa.

Andexanet alfa is a recombinant form of human factor Xa protein which binds specifically to apixaban and rivaroxaban, thereby reversing their anticoagulant effects.

NICE guidance TA697 (updated 15 January 2025) - Andexanet alfa for reversing anticoagulation from apixaban or rivaroxaban - recommends that andexanet alfa should only be used in life-threatening or uncontrolled bleeding in adults where the bleed is in the gastrointestinal tract.

SMC No. SMC2273 - Andexanet alfa use for adult patients treated with a direct factor Xa (FXa) inhibitor (apixaban or rivaroxaban) when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding – recommended its use in life-threatening or uncontrolled bleeding on an interim basis in 2020; this is subject to ongoing evaluation and future reassessment.

Published, peer reviewed studies, show that andexanet alfa is effective at reducing anti-factor Xa activity to a greater extent than placebo and appears to restore thrombin generation[1]. Additionally, in patients with intracranial haemorrhage, andexanet alfa demonstrates a reduction in haematoma expansion; however, there appears to be no difference in 30-day mortality and long-term neurological outcomes are unknown. Significant increases in rates of thrombotic events and ischemic strokes have also been noted with the use of andexanet alfa[2]. A recent systematic review comparing andexanet alfa to prothrombin complex concentrate (4 factor PCC) showed no mortality benefit but increased thrombotic events with andexanet alfa[3].

Whilst andexanet alfa reverses the effects of direct factor Xa inhibitors and has therefore been recommended in the management of uncontrolled major haemorrhage in those taking apixaban or rivaroxaban, the increase in thrombotic complications following its use is significant.

The decision to use andexanet alfa is clearly both complex and multifactorial. Factors that may influence decision making include access to blood products, including PCC, underlying pathological processes (i.e. blunt or penetrating trauma) and speed at which surgical, or interventional radiological,

haemorrhage control is likely to be achieved. A multidisciplinary approach is needed, including input from the emergency department, critical care, surgery and haematology.

Recommendation

With the current available evidence, and pending updated advice from the Scottish Medicines Consortium, the STN does not recommend the *routine* use of andexanet alfa in those patients on apixaban or rivaroxaban with life-threatening traumatic major haemorrhage. This is particularly true where there is significant blood product resource available (including PCC) and a reasonable likelihood of rapid surgical, or interventional radiological, haemorrhage control. Andexanet alfa should not be considered in those on a prophylactic dose regimen of apixaban or rivaroxaban.

In cases where definitive haemorrhage control is not an option or unsuccessful (often associated with blunt trauma), andexanet alfa could be considered as a therapeutic option, following multidisciplinary discussion, when death from exsanguination is a likely outcome.

References:

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2. SJ Connolly, M Sharma, AT Cohen et al. Andexanet for Factor Xa Inhibitor–Associated Acute Intracerebral Hemorrhage. N Engl J Med, May 2024;390:1745-1755. DOI: 10.1056/NEJMoa2313040

3. D Orso, F Fonda, A Brussa et al. Andexanet alpha versus four-factor prothrombin complex concentrate in DOACs anticoagulation reversal: an updated systematic review and meta-analysis. Crit Care, Jul 24;28(1):221. DOI: 10.1186/s13054-024-05014-x