NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Andexanet alfa for reversing anticoagulation from apixaban or rivaroxaban in people with intracranial haemorrhage (part review of TA697)

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of andexanet alfa within its marketing authorisation for reversing anticoagulation from apixaban or rivaroxaban in people with intracranial haemorrhage.

Background

Anticoagulant therapy is used for preventing and treating thromboembolism across various clinical indications, including the treatment and secondary prevention of deep vein thrombosis (DVT), pulmonary embolism (PE) and after orthopaedic surgery for the prevention of venous thromboembolism as well as to prevent stroke and systemic embolism in patients with non-valvular atrial fibrillation. Direct oral anticoagulants (DOACs) act by inhibiting specific components of the coagulation cascade, such as factor Xa (apixaban, edoxaban, rivaroxaban) or thrombin (dabigatran). Major bleeding events are potential adverse effects of anticoagulants. Antidotes are needed to reverse anticoagulation in case of life-threatening bleeding.

In England, between 2021 and 2022 there were around 12.5 million prescriptions dispensed in the community for apixaban, and rivaroxaban.[1] It is estimated that major bleeding with factor Xa inhibitors ranges from 1-3% and that intracranial haemorrhage rates range from 0.3-0.5%, based on clinical trial results.[2,3]

NICE technology appraisal TA697 recommends andexanet alfa as an option for reversing anticoagulation from apixaban or rivaroxaban in adults with life-threatening or uncontrolled bleeding if the bleed is in the gastrointestinal tract. The guidance also includes an ‘only in research recommendation’ for reversing anticoagulation from apixaban or rivaroxaban in adults with life-threatening or uncontrolled bleeding in the skull (intracranial haemorrhage), in the form of an ongoing randomised trial mandated by the regulator. This partial review will appraise andexanet alfa for the population for whom it is currently recommended for use only in research.

Current treatment for anticoagulation reversal from apixaban or rivaroxaban in people with intracranial haemorrhage is established clinical management which may include prothrombin complex concentrate, used off label with or without tranexamic acid.

The technology

Andexanet alfa (Ondexxya, AstraZeneca) is indicated for adult patients treated with a direct factor Xa inhibitor (apixaban or rivaroxaban) when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.

Intervention(s)	Andexanet alfa
Population(s)	Adults needing reversal of anticoagulation from apixaban or rivaroxaban for life-threatening or uncontrolled bleeding in the skull (intracranial haemorrhage)
Comparators	Established clinical management of uncontrolled or life-threatening bleeding without andexanet alfa (including prothrombin complex concentrate with or without tranexamic acid)
Outcomes	The outcome measures to be considered include: • requirement for blood products • control of bleeding • change in size of intracranial bleeding • neurological outcomes • hospital stay • mortality • adverse effects of treatment (including thrombotic events) • health related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Andexanet alfa for reversing anticoagulation from apixaban or rivaroxaban (2021) NICE technology appraisal guidance [TA697]. **Related NICE guidelines:** Major trauma: assessment and initial management (2016). [NG39].
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019)

Questions for consultation

What does established clinical management without andexanet alfa include (specifically for reversing anticoagulation from apixaban or rivaroxaban in people with intracranial haemorrhage)?

Do you consider that the use of andexanet alfa can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Are the outcomes listed in the scope appropriate (specifically in people with intracranial haemorrhage)? Do any other outcomes need to be included?

Are there any subgroups of people in whom andexanet alfa is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Would andexanet alfa be a candidate for managed access?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which the treatment will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1 NHS Business Services Authority Prescription Cost Analysis – England, 2021/22. Accessed October 2023

2 Piccini JP et al. (2014) Management of major bleeding events in patients treated with rivaroxaban vs. warfarin: results from the ROCKET AF trial. European Heart Journal (2014) 35, 1873–1880.

3 Granger CB et al. (2011) Apixaban versus Warfarin in Patients with Atrial Fibrillation. N Engl J Med 2011;365:981-92.