NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA245; Apixaban for the prevention of venous thromboembolic events in the knee and hip

This guidance was issued in January 2012.

The review date for this guidance is January 2015.

1. Recommendation

TA245 should be transferred to the 'static guidance list'. That we consult on this proposal.

2. Original remit

To appraise the clinical and cost effectiveness of apixaban, within its licensed indication, for the prevention of venous thromboembolism in people undergoing elective knee and hip replacement surgery.

3. Current guidance

1.1. Apixaban is recommended as an option for the prevention of venous thromboembolism in adults after elective hip or knee replacement surgery.

4. Rationale[1]

No new or ongoing clinical studies have been found that would suggest an update of the guidance is required.

5. Implications for other guidance producing programmes

NICE's Clinical Guidelines Updates Team is currently updating a discreet section the clinical guideline 92 "Venous thromboembolism – reducing the risk". This update will consider the effectiveness of mechanical VTE prophylaxis in people with stroke who are in hospital.

In addition, a substantial update of CG92 was agreed by Guidance Executive in July 2014. It is anticipated that the update will be commissioned into the clinical guidelines programme in May 2015. The scoping process for the update will include an assessment of the relationships between the clinical guideline and other relevant NICE guidance including this specific technology appraisal.

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

6. New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from February 2009 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

The marketing authorisations for apixaban and its comparators (dabigatran etexilate, rivaroxaban, fondaparinux and low molecular weight heparin) for preventing venous thromboembolism after total hip of total knee replacement have not changed since the publication of technology appraisal 245. There are no new technologies that are indicated for the prevention of venous thromboembolism after total hip or total knee replacement in adults.

There have been no further randomised controlled trials or cohort studies assessing apixaban in this indication since technology appraisal 245.

The review decisions for technology appraisals 157 (dabigatran etexilate for the prevention of venous thromboembolism after hip and knee replacement) in 2011, and 170 (rivaroxaban for the prevention of venous thromboembolism after total hip or total knee replacement in adults) in 2012 were that both guidance documents should be placed on the static list. A review of clinical guideline 92: venous thromboembolism- reducing the risk is currently ongoing. During the consultation on the review proposal for this guideline stakeholders stated that the updated guideline should cross-reference technology appraisal 245.

The cost of apixaban now is approximately a third lower than at the time of the appraisal. The quoted prices for apixaban in technology appraisal 245 were £17.15 for 10 tablets; £34.30 for 20 tablets and £102.90 for 60 tablets. The current NHS list prices for apixaban are £10.98 for 10 tablets, £21.96 for 20 tablets, £65.90 for 60 tablets (BNF accessed November 2014).

8. Implementation

No submission was received from Implementation.

9. Equality issues

No equalities issues were raised in Technology Appraisal No. 245.

GE paper sign off: Janet Robertson, 9 January 2015

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Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the [specify STA or MTA] process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed

- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

NICE Pathway Venous thromboembolism. Last revised June 2014.

Venous thromboembolism: reducing the risk. NICE clinical guideline 92 (2010). Review decision July 2014: to update the guideline.

Dabigatran etexilate for the prevention of venous thromboembolism after hip or knee replacement surgery in adults. NICE technology appraisal guidance 157 (2008). Status: transferred to static guidance August 2011.

Rivaroxaban for the prevention of venous thromboembolism after total hip or total knee replacement surgery in adults. NICE technology appraisal guidance 170 (2009). Status: transferred to static guidance May 2012.

Details of changes to the indications of the technology

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
"The recommended dosage of apixaban in the summary of product characteristics is 2.5 mg orally twice daily. The initial dose should be taken 12–24 hours after surgery. Recommended treatment durations are 32–38 days for patients having hip replacement surgery and 10–14 days for patients having knee replacement surgery." "Apixaban costs £17.15, £34.30 and £102.90 for packs of 10, 20 and 60 tablets respectively excluding VAT (NHS list price as reported by the manufacturer). The cost of treatment is estimated to be £41.16 (based on 12 days' treatment) for knee replacement surgery and £116.62 for hip replacement surgery (based on 34 days' treatment)."	The dosage and suggested duration is the same as the original guidance. Source: SPC, accessed 13 Nov 14. Current price: Apixaban 2.5 mg, net price 10-tab pack = £10.98, 20-tab pack = £21.96, 60-tab pack = £65.90; 5 mg, 56-tab pack = £61.50 Source: eBNF, accessed 13 Nov 14.

Registered and unpublished trials

Trial name and registration number	Details
A Phase IV, Open-Label, Multi-center Study to Evaluate the Safety of Apixaban in Indian Subjects Undergoing Elective Total Knee Replacement or Total Hip Replacement Surgery. NCT01884337 CV185-158	Phase IV, participant recruitment 'suspended'. Estimated enrolment: 500 Primary completion date: March 2016.
Eliquis (Apixaban) Regulatory Post Marketing Surveillance in Clinical Practice for Venous Thromboembolism (VTE) Prevention NCT01885585 CV185-222	Not yet recruiting. Estimated enrolment: 3000 Primary completion date: December 2016. *"The objective of this regulatory Post-Marketing Surveillance in Korea is to reconfirm the clinical usefulness of Eliquis through collecting, reviewing, identifying and verifying the safety and effectiveness information about Eliquis in general practice"* *The patient cohorts for this observational study are:* • *Patients with risk of VTE* • *Patients undergoing elective total hip replacement arthroplasty or elective total knee replacement arthroplasty and signed on the data release*