

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA249; ‘Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation’, TA256; ‘Rivaroxaban for the prevention of stroke in atrial fibrillation and ‘Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation’ (publication anticipated in February 2013)

This guidance was issued in:

TA249 – March 2012

TA256 – May 2012

Apixaban – it is expected that the FAD will be published in January and, if there are no appeals, publication of the final guidance is expected in February 2013.

The review date for this guidance is:

TA249 – October 2014

TA256 – October 2014

Apixaban – the FAD states that *“The guidance on this technology will be considered for review alongside the related technology appraisals TA249 and TA256”*.

1. Recommendation

The recommendations of TA249 and TA256 and the recommendations on apixaban will be incorporated, verbatim, into the ongoing update of clinical guideline 36 ‘Atrial fibrillation’.

The technology appraisals will be moved to the static list and will remain extant when the guideline is published. This has the consequence of preserving the funding direction.

That we consult on this proposal.

2. Original remit(s)

TA249:

To appraise the clinical and cost-effectiveness of dabigatran etexilate within its licensed indication for the prevention of stroke and systemic embolism in people with atrial fibrillation.

TA256:

To appraise the clinical and cost effectiveness of rivaroxaban within its licensed indication for the prevention of stroke and non-central nervous system (CNS) systemic embolism in people with non-valvular atrial fibrillation.

Apixaban

To appraise the clinical and cost effectiveness of apixaban within its licensed indication for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation with one or more risk factors for stroke or systemic embolism.

3. Current guidance**TA249:**

1.1 Dabigatran etexilate is recommended as an option for the prevention of stroke and systemic embolism within its licensed indication, that is, in people with nonvalvular atrial fibrillation with one or more of the following risk factors:

- previous stroke, transient ischaemic attack or systemic embolism left ventricular ejection fraction below 40%
- symptomatic heart failure of New York Heart Association (NYHA) class 2 or above
- age 75 years or older
- age 65 years or older with one of the following: diabetes mellitus, coronary artery disease or hypertension.

1.2 The decision about whether to start treatment with dabigatran etexilate should be made after an informed discussion between the clinician and the person about the risks and benefits of dabigatran etexilate compared with warfarin. For people who are taking warfarin, the potential risks and benefits of switching to dabigatran etexilate should be considered in light of their level of international normalised ratio (INR) control.

TA256:

1.1 Rivaroxaban is recommended as an option for the prevention of stroke and systemic embolism within its licensed indication, that is, in people with nonvalvular atrial fibrillation with one or more risk factors such as:

- congestive heart failure
- hypertension
- age 75 years or older
- diabetes mellitus,
- prior stroke or transient ischaemic attack.

1.2 The decision about whether to start treatment with rivaroxaban should be made after an informed discussion between the clinician and the person about the risks and benefits of rivaroxaban compared with warfarin. For people who are taking warfarin, the potential risks and benefits of switching to rivaroxaban

should be considered in light of their level of international normalised ratio (INR) control.

4. Apixaban provisional guidance

1.1 Apixaban is recommended as an option for preventing stroke and systemic embolism within its marketing authorisation, that is, in people with nonvalvular atrial fibrillation with 1 or more risk factors such as:

- prior stroke or ischaemic attack
- age 75 years or older
- hypertension
- diabetes mellitus
- symptomatic heart failure.

1.2 The decision about whether to start treatment with apixaban should be made after an informed discussion between the clinician and the person about the risks and benefits of apixaban compared with warfarin, dabigatran etexilate and rivaroxaban. For people who are taking warfarin, the potential risks and benefits of switching to apixaban should be considered in light of their level of international normalised ratio (INR) control.

5. Rationale¹

These technology appraisals overlap with the remit of an ongoing update of a clinical guideline. There is also a related quality standard.

There are no new or ongoing studies that would be expected to change the recommendations. There are no direct comparisons of the drugs. Several indirect comparisons have been published. These rely on the same evidence base as was used for the development of TA249, TA256 and for the ongoing appraisal of apixaban for this indication. A related drug, apixaban was discussed by the appraisal committee on 20th November 2012. This resulted in the Committee recommending apixaban as an option within its licensed indication for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation.¹ The FAD is expected to be published in January, with final guidance in February 2013 assuming that there is no appeal.

Given the lack of new evidence and evidence from trials that compare the drugs with each other directly, it is unlikely that a review conducted through the multiple technology appraisal process would be able to distinguish more clearly between the newer anticoagulants on the basis of clinical and cost effectiveness than was possible in the three separate single technology appraisals. It is likely that the guidance would not change and that all three novel anticoagulants would remain recommended as options. There may be other reasons for choosing one drug over another in particular situations, and these may flow from the contextualisation which the guideline update will provide.

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

This review proposal has been prepared taking into account the principles outlined in the Department of Health policy document PWG IB (10)05. These criteria are outlined in 'Appendix 1'. The purpose of these criteria is to preserve the funding direction for the recommendations in NICE technology appraisals where it remains necessary.

6. Implications for other guidance producing programmes

The Centre for Clinical Practice would welcome a consultation on the proposal that TA249 (Dabigatran etexilate for the prevention of stroke in atrial fibrillation) and TA256 (Rivaroxaban for the prevention of stroke in atrial fibrillation) and the forthcoming technology appraisal of apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation should be incorporated into the updated guideline on the management of atrial fibrillation. This update is currently early in development, so that, if the ultimate decision is in line with the proposal, there will be no difficulty in implementing the decision.

7. 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 December 2008 (TA249) and January 2010 (TA256) 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.

8. Summary of evidence and implications for review

The marketing authorisations for dabigatran etexilate and rivaroxaban have not changed since the publication of the respective guidance TA249 and TA256. Dabigatran etexilate and rivaroxaban were both recommended for the prevention of stroke and/or systemic embolism in line with their marketing authorisations. There have been no amendments to the marketing authorisations for the comparators included in the guidance.

No new interventions have come to market since the original guidance was issued, however it is worth noting that the technology appraisal of Apixaban for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation with one or more risk factor for stroke or systemic embolism is currently in development (published guidance expected April 2013).

Technology appraisals 249 and 256 were published in March and May 2012 respectively. The majority of studies identified related to the studies considered in these appraisals. For dabigatran etexilate, 16 publications related to the RE-LY study were identified the majority of which were published before the publication of TA249. A new subgroup-analysis of the RE-LY trial was provided by Boehringer Ingelheim which investigated the outcomes associated with different sites of intracranial bleeding occurring with warfarin versus dabigatran etexilate (Hart et al. 2012). The absence of an antidote to reverse dabigatran etexilate's anticoagulant effect has prompted concern that intracranial haemorrhages with dabigatran etexilate could

carry a worse prognosis than could those associated with warfarin. This study concluded that the clinical spectrum of intracranial haemorrhage was similar for patients given warfarin and dabigatran etexilate, while absolute rates at all sites and both fatal and traumatic intracranial haemorrhages were lower with dabigatran etexilate than with warfarin.

For rivaroxaban, 5 publications were identified, all of which related to the ROCKET-AF study which compared rivaroxaban with warfarin.

Several systematic reviews and indirect comparisons have been published since the publication of TA249 and TA256. All of these were in agreement that the new oral anticoagulants (dabigatran etexilate, rivaroxaban and apixaban) are more efficacious than warfarin in preventing stroke and systemic embolism in patients with atrial fibrillation (Baker et al. 2012; Harenberg et al 2012; Klein et al 2012; Miller et al 2012; Testa et al. 2012) However, two studies highlighted that there may be significant differences in efficacy and safety parameters between dabigatran etexilate, rivaroxaban (and apixaban) and that head-to-head clinical trials are required to confirm this (Baker et al. 2012; Harenberg et al 2012).

Four economic analyses were identified for dabigatran etexilate, two of which are UK-specific (Kansal et al 2012^a (provided by Boehringer Ingelheim); Pink et al. 2011) and one which compared dabigatran etexilate with rivaroxaban in a Canadian setting (Kansal et al 2012^b). Of the UK specific analyses, Kansal et al. (2012^a) concluded that dabigatran etexilate is likely to be cost-effective for the prevention of stroke and systemic embolism in eligible UK patients with atrial fibrillation. Pink et al. (2011) concluded that dabigatran etexilate 150 mg twice daily could be cost-effective compared with warfarin, but this was uncertain, while the low-dose dabigatran etexilate (110 mg twice daily) was not cost-effective compared with warfarin. However, the analysis by Pink et al. (2011) did not reflect the licensed indication and therefore how dabigatran would be used in clinical practice since the higher dose (150 mg twice daily) dabigatran would only be used in people with atrial fibrillation who are 80 years and under, and the lower dose (110 mg twice daily) in people who are 80 years or older.

Since publication of TA249, the manufacturer of dabigatran etexilate (Boehringer Ingelheim) has announced a 13% reduction in the price from £2.52 per day to £2.20 per day from 1st April 2012.² Since TA249 recommends the use of dabigatran etexilate as an option for the prevention of stroke and systemic embolism in people with nonvalvular atrial fibrillation (within its licensed indication), a reduction in price does not impact upon the existing recommendation in the guidance.

In conclusion, there is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of either of dabigatran etexilate or rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation. Therefore, it would be appropriate to incorporate TA249 and TA256 into the on-going update of clinical guideline 36 (CG36). However, an update of the guideline must be

² Dabigatran price reduction. http://www.pharmatimes.com/Article/12-03-29/B-I_cuts_Pradoxal_s_price_by_13.aspx

mindful of the timings of the ongoing technology appraisal of apixaban for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation with one or more risk factor for stroke or systemic embolism (published guidance expected April 2013).

9. Implementation

A submission from Implementation is included in Appendix 3.

Because of the very recent publication of TA249 and TA 256, the implementation advice received cannot fully be interpreted for the indications considered as part of these appraisals in terms of adherence to NICE guidance because data is only available on the period prior to release of the technology appraisal guidance. Therefore it is not possible, based on the available data, to comment on whether current practice has changed since the original guidance.

10. Equality issues

The Committee concluded that there were no equality issues that needed addressing in the guidance in either appraisal.

GE paper sign off: Janet Robertson – Associate Director, 30 October 2012

Contributors to this paper:

Information Specialist:	Toni Price
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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.	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.	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.	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.	<p>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.</p> <p>This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.</p>	Yes

Options	Consequence	Selected – ‘Yes/No’
The guidance should be updated in an on-going clinical guideline.	<p>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.</p> <p>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).</p>	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

TA197 Dronedaronone for the treatment of non-permanent atrial fibrillation. Issued August 2010. Review date: Originally March 2013, but in July 2012 NICE proposed a change in wording to reflect the change in the marketing authorisation, and for TA197 to be “incorporated into the ongoing update of NICE clinical guideline 36 Atrial fibrillation”.

CG36 Management of atrial fibrillation. Issued June 2006. Review decision August 2011: to update, and work is in progress.

In terms of the technologies, we have issued guidance on:

- Rivaroxaban for the prevention of venous thromboembolism (TA170)
- Rivaroxaban for the treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism (TA261)
- Dabigatran etexilate for the prevention of venous thromboembolism after hip or knee replacement surgery in adults (TA157)

In progress

Apixaban for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation with one or more risk factor for stroke or systemic embolism. Technology Appraisal. Expected date of issue: April 2013. In May 2012 the webpage was updated to say “Following on from advice received from the manufacturer, this appraisal has been rescheduled to align with latest regulatory expectations. Therefore, we now anticipate that the appraisal will begin during late June 2012”.

In terms of the technologies, we have the following in progress:

- Rivaroxaban for the treatment of acute symptomatic pulmonary embolism with or without symptomatic deep vein thrombosis and the prevention of recurrent venous thromboembolic events. Expected date of issue: July 2013.
- Rivaroxaban for the prevention of adverse outcomes in patients after the acute management of acute coronary syndrome. Expected date of issue: September 2013.

Referred - Qs and CGs

Quality Standard: Atrial Fibrillation is listed on the NICE website as ‘referred to NICE in March 2012’.

Suspended/terminated

Ximelagatran for the treatment and prevention of stroke and other thromboembolic complications associated with atrial fibrillation. Terminated 2006: "The manufacturer of ximelagatran has advised us that they have withdrawn regulatory applications in relation to this product following receipt of trial data."

Atrial fibrillation - idraparinux sodium. Suspended July 2007: "The manufacturer of idraparinux sodium has advised us that the regulatory strategy in relation to this product is not finalised".

Clopidogrel in combination with aspirin for the prevention of vascular events in people with atrial fibrillation. Discontinued February 2011 following "information received from the manufacturers in relation to this indication".

Vernakalant for the treatment of rapid conversion of recent onset atrial fibrillation. Suspended June 2011 "following on from information received from the manufacturer, regarding the timings of the launch of the product in the UK."

In terms of the technologies, the following are suspended:

- Dabigatran etexilate for the treatment of acute venous thromboembolic events. Suspended December 2010. "Following on from advice received from the manufacturer, dates for this appraisal will be confirmed once regulatory approval timelines are established."
- Rivaroxaban for the prevention of venous thromboembolism in people hospitalised for acute medical conditions. Suspended June 2012 as the manufacturer "is not currently pursuing a licensing application for rivaroxaban in this indication".

Details of changes to the indications of the technology

Indication considered in original appraisal	Proposed indication (for this appraisal)
<p>Dabigatran etexilate has a UK marketing authorisation for the 'prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation with one or more of the following risk factors:</p> <ul style="list-style-type: none"> • previous stroke, transient ischaemic attack, or systemic embolism • left ventricular ejection fraction below 40% • symptomatic heart failure of New York Heart Association (NYHA) class 2 or above • age 75 years or over • age 65 years or over with one of the following: diabetes mellitus, coronary artery disease, or hypertension'. 	<p>Unchanged for this indication</p>
<p>Rivaroxaban has a UK marketing authorisation for the 'prevention of stroke and systemic embolism in adult patients with non valvular atrial fibrillation with one or more risk factors such as: congestive heart failure, hypertension, age 75 years or older, diabetes mellitus, prior stroke or transient ischaemic attack'.</p>	<p>Unchanged for this indication</p>

Details of new products

Drug (manufacturer)	Details (phase of development, expected launch date,)
<p>Edoxaban tosylate for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation (Daiichi Sankyo)</p>	<p>New Drugs Online gives an expected launch date of Q3 2013.</p>

Registered and unpublished trials

Trial name and registration number	Details
<p>NCT01674647 A Prospective, Randomized, Open-label, Parallel-group, Active-controlled, Multicenter Study Exploring the Efficacy and Safety of Once-daily Oral Rivaroxaban (BAY59-7939) Compared With That of Dose-adjusted Oral Vitamin K Antagonists (VKA) for the Prevention of Cardiovascular Events in Subjects With Nonvalvular Atrial Fibrillation Scheduled for Cardioversion</p>	<p>Phase III, not yet open for recruitment. Estimated enrollment: 1500 Study start date: September 2012 Estimated primary completion date: December 2013. Estimated study completion date: December 2013.</p>
<p>NCT00808067 RELY-ABLE Long Term Multi-center Extension of Dabigatran Treatment in Patients With Atrial Fibrillation Who Completed the RE-LY Trial and a Cluster Randomised Trial to Assess the Effect of a Knowledge Translation Intervention on Patient Outcomes</p>	<p>Phase III, ongoing not recruiting. Enrollment: 6200 Study start date: November 2008. Estimated primary completion date: April 2013.</p>
<p>NCT01546883 Dabigatran-related Effect on Progression of Atrial Fibrosis in Patients With Atrial Fibrillation</p>	<p>Phase IV, currently recruiting. Enrollment: 30 Study start date: February 2012. Estimated primary completion date: March 2013.</p>
<p>NCT01339819 Impact of Dabigatran and Phenprocoumon on ADP Induced Platelet Aggregation in Patients With Atrial Fibrillation</p>	<p>Phase IV, currently recruiting. Enrollment: 70 Study start date: April 2011. Estimated primary completion date: May 2012.</p>
<p>NCT01493557 A Prospective, Open Label Study Evaluating the Efficacy of Two Management Strategies (Pantoprazole 40 mg q.a.m. and Taking Pradaxa® With Food (Within 30 Minutes After a Meal) on Gastrointestinal Symptoms (GIS) in Patients Newly on Treatment With Pradaxa® 150 mg b.i.d. or 75 mg b.i.d. for the Prevention of Stroke and Systemic Embolism in Patients With Non-valvular Atrial Fibrillation (NVAf)</p>	<p>Phase IV, currently recruiting. Enrollment: 1200 Study start date: December 2011. Estimated primary completion date: December 2013.</p>

Trial name and registration number	Details
NCT01352702 Impact of Dabigatran and Phenprocoumon on Clopidogrel Mediated ADP Induced Platelet Aggregation in Patients With Atrial Fibrillation	Phase IV, currently recruiting. Enrollment: 70 Study start date: May 2011. Estimated primary completion date: February 2013.
NCT01468155 Dabigatran for Peri Procedural Anticoagulation During Radiofrequency Ablation of Atrial Fibrillation	Phase IV, not yet open for recruiting. Enrollment: 200 Study start date: November 2011. Estimated primary completion date: January 2013.

References

Baker, W. L. and O. J. Phung. (2012). Systematic review and adjusted indirect comparison meta-analysis of oral anticoagulants in atrial fibrillation." Circulation Cardiovascular.5 (2012): 711-19.

Harenberg, J., et al. (2012). Comparison of efficacy and safety of dabigatran, rivaroxaban and apixaban in patients with atrial fibrillation using network meta-analysis." International Angiology 31.4: 330-39.

Hart, R. G., et al. (2012). Intracranial hemorrhage in atrial fibrillation patients during anticoagulation with warfarin or dabigatran: the RE-LY trial." Stroke 43.6: 1511-17.

Kansal,A.R.; Sorensen,S.V.; Gani,R.; Robinson,P.; Pan,F.; Plumb,J.M.; Cowie,M.R. (2012) Cost-effectiveness of dabigatran etexilate for the prevention of stroke and systemic embolism in UK patients with atrial fibrillation. Heart 98:573 – 578

Kansal,A.R.; Sharma,M.; Bradley-Kennedy,C.; Clemens,A.; Monz,B.U.; Peng,S.; Roskell,N.; Sorensen,S.V. (2012). Dabigatran versus rivaroxaban for the prevention of stroke and systemic embolism in atrial fibrillation in Canada. Comparative efficacy and cost-effectiveness Thrombosis and Haemostasis 108.4: 672-682.

Klein, L. (2012) Review: New oral anticoagulants reduced stroke and systemic embolism compared with warfarin in AF." Annals of Internal Medicine 157.6: JC3-2.

Miller, C. S., et al.(2012). Meta-analysis of efficacy and safety of new oral anticoagulants (dabigatran, rivaroxaban, apixaban) versus warfarin in patients with atrial fibrillation." American Journal of Cardiology 110.3: 453-60.

Pink, J., et al. (2011) Dabigatran etexilate versus warfarin in management of non-valvular atrial fibrillation in UK context: quantitative benefit-harm and economic analyses (Structured abstract)." SO: BMJ 343:d6333.3.

Testa, L., et al. (2012). Adjusted indirect comparison of new oral anticoagulants for stroke prevention in atrial fibrillation." Qjm 105.10: 949-57.

Appendix 3 – Implementation submission

Implementation feedback: review of NICE technology appraisal 249 & 256

NICE Technology Appraisal 249 Dabigatran etexilate for the prevention of stroke in atrial fibrillation

NICE Technology Appraisal 256 Rivaroxaban for the prevention of stroke in atrial fibrillation

Implementation input required by 11/09/2012

Please contact Rebecca Lea regarding any queries

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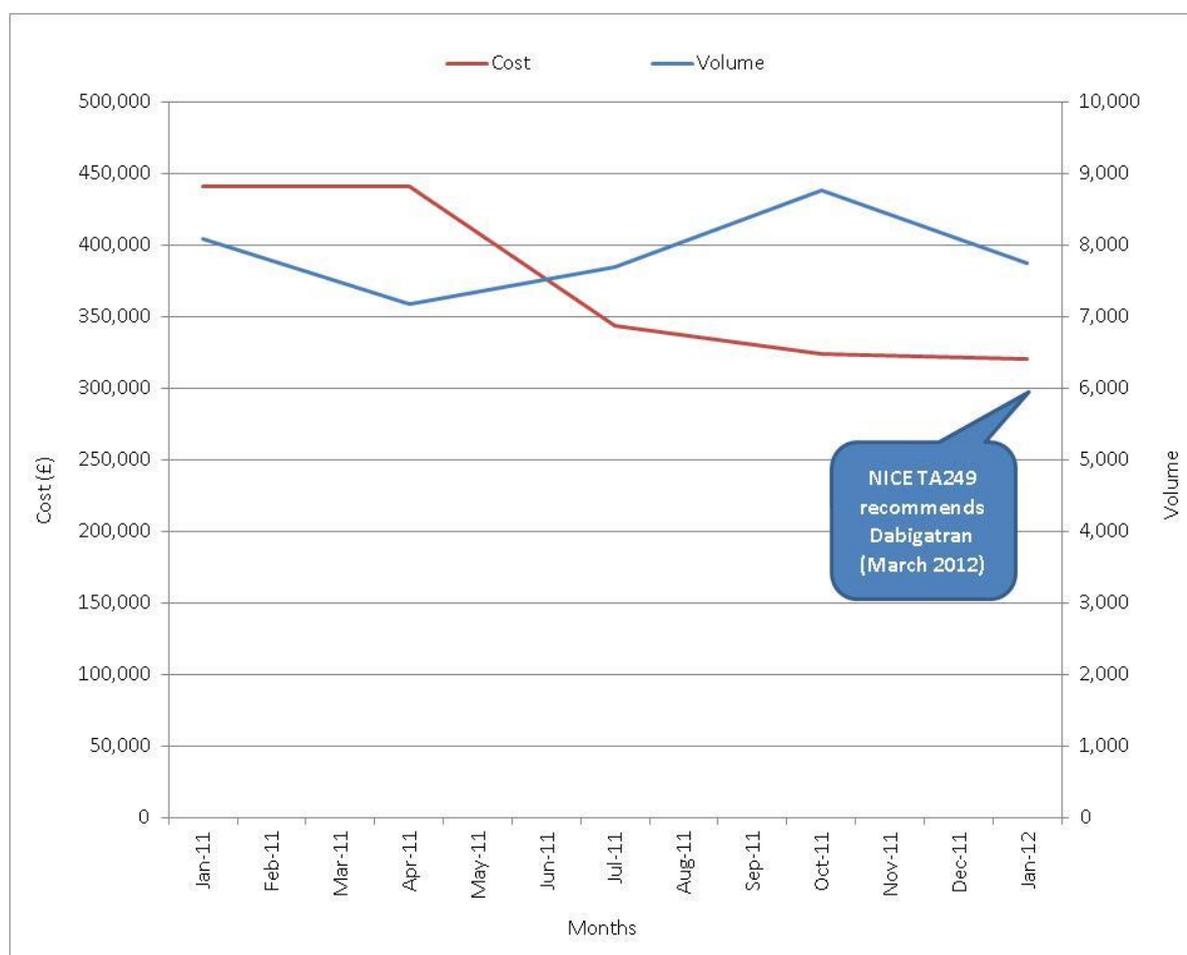
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1 Routine healthcare activity data

1.1 Hospital Pharmacy Audit Index

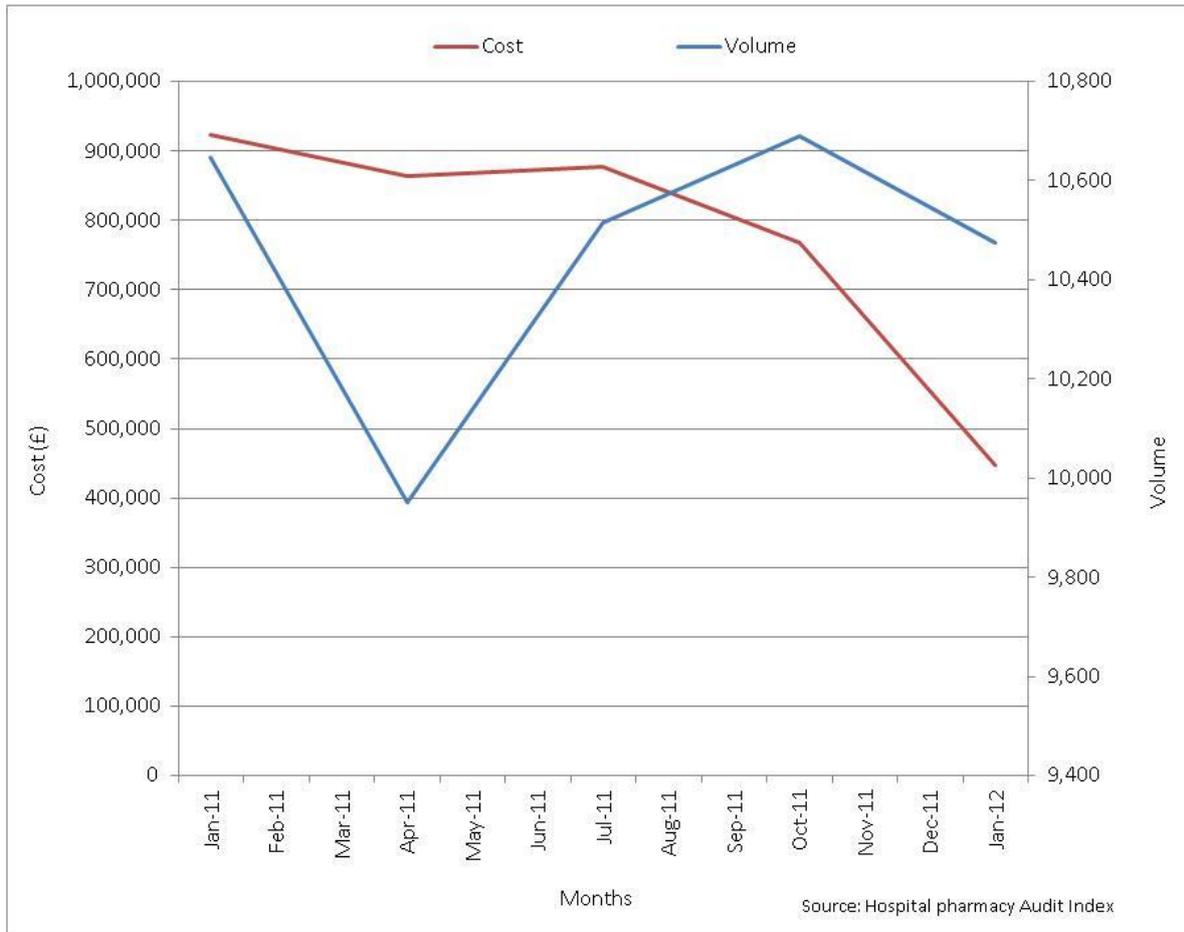
This section presents Hospital Pharmacy Audit Index data on the net ingredient cost (NIC) and volume of Dabigatran and Rivaroxaban prescribed and dispensed by hospital pharmacies for use in hospitals in England between January 2011 and March 2012.

Figure 1 Cost and volume of Dabigatran prescribed and dispensed in hospitals between January 2011 and March 2012



Note: NICE Technology Appraisal 157, which recommends Dabigatran for the prevention of venous thromboembolism after hip or knee replacement surgery in adults, was published in September 2008.

Figure 2 Cost and volume of Rivaroxaban prescribed and dispensed in hospitals between January 2011 and March 2012



Note: NICE Technology Appraisal 256, which recommends Rivaroxaban for the prevention of stroke in atrial fibrillation, was published in May 2012.

NICE Technology Appraisal 170, which recommends Rivaroxaban for the prevention of venous thromboembolism after total hip or total knee replacement in adults, was published in April 2009.

NICE Technology Appraisal 261, which recommends Rivaroxaban for the prevention of recurrent deep vein thrombosis and pulmonary embolism, was published in July 2012.

1.2 ePACT and hospital ePACT

This section presents the net ingredient cost (NIC) and the number of prescriptions items of Dabigatran and Rivaroxaban prescribed in primary care and hospitals that have been dispensed in the community in England between July 2007 and June 2012.

Figure 3 Cost and number of items of Dabigatran prescribed in primary care and hospitals that have been dispensed in the community

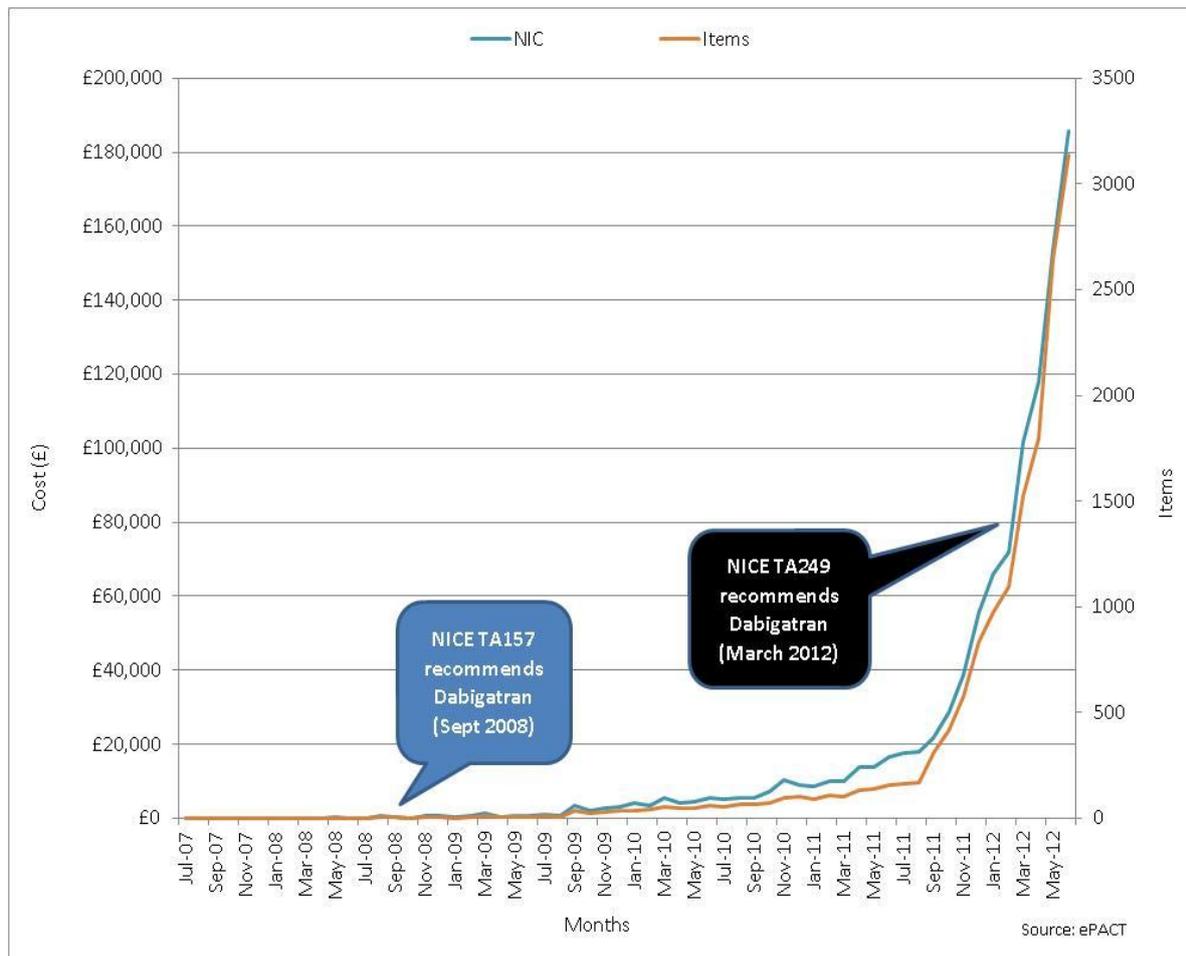
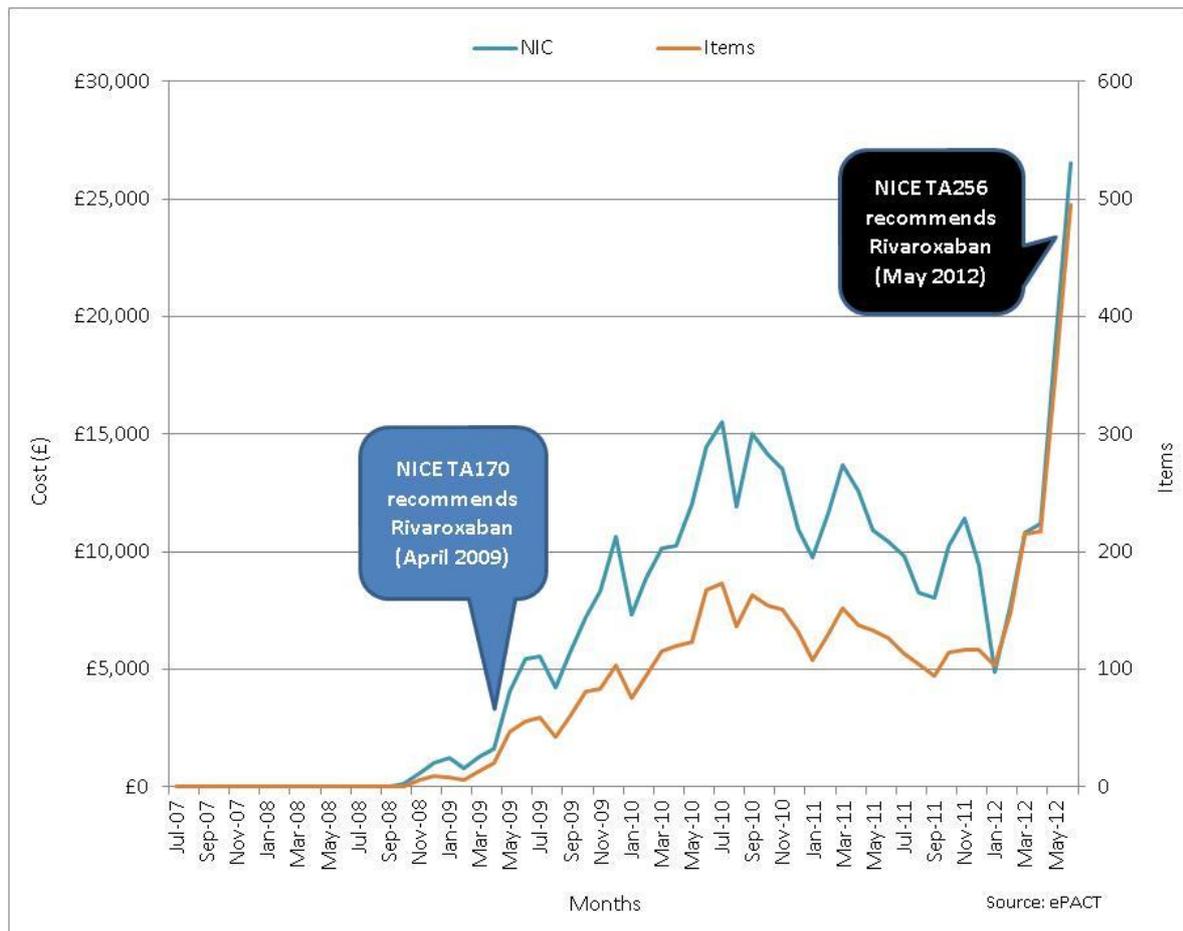


Figure 4 Cost and number of items of Rivaroxaban prescribed in primary care and hospitals that have been dispensed in the community



NICE Technology Appraisal 261, which recommends Rivaroxaban for the prevention of recurrent deep vein thrombosis and pulmonary embolism was published in July 2012.

2 Implementation studies from published literature

Information is taken from the uptake database ([ERNIE](#)) website.

Nothing to add at this time.

3 Qualitative input from the field team

The implementation field team have recorded the following feedback in relation to this guidance:

One person expressed surprise at the positive recommendation for the use of dabigatran etexilate for the prevention of stroke and systematic embolism in atrial fibrillation, as their local view is that if this recommendation is contained in the final guidance this will push up anti-embolitic prescribing costs without delivering any significant clinical gain. Another person expressed concern over the recommendation for Dabigatran in AF, and worried over increased costs and monitoring requirements.

Appendix A: Healthcare activity data definitions

Prescribing analysis and cost tool system

This information comes from the electronic prescribing analysis and cost tool (ePACT) system, which covers prescriptions by GPs and non-medical prescribers in England and dispensed in the community in the UK. The Prescription Services Division of the NHS Business Services Authority maintains the system. PACT data are used widely in the NHS to monitor prescribing at a local and national level. Prescriptions written in hospitals but dispensed in the community (FP10 [HP]) are not included in PACT data. Prescriptions dispensed in hospitals or mental health units, and private prescriptions, are not included in PACT data.

Measures of prescribing

Prescription Items: Prescriptions are written on a prescription form. Each single item written on the form is counted as a prescription item. The number of items is a measure of how many times the drug has been prescribed.

Cost: The net ingredient cost (NIC) is the basic price of a drug listed in the drug tariff, or if not in the drug tariff, the manufacturer's list price.

Data limitations (national prescriptions)

PACT data do not link to demographic data or information on patient diagnosis.

Therefore the data cannot be used to provide prescribing information by age and sex or prescribing for specific conditions where the same drug is licensed for more than one indication.

IMS HEALTH Hospital Pharmacy Audit Index (IMS HPAI)

IMS HEALTH collects information from pharmacies in hospital trusts in the UK. The section of this database relating to England is available for monitoring the overall usage in drugs appraised by NICE. The IMS HPAI database is based on issues of medicines recorded on hospital pharmacy systems. Issues refer to all medicines

supplied from hospital pharmacies: to wards; departments; clinics; theatres; satellite sites and to patients in outpatient clinics and on discharge.

Measures of prescribing

Volume: The HPAI database measures volume in packs and a drug may be available in different pack sizes and pack sizes can vary between medicines.

Cost: Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Costs based on the drug tariff provide a degree of standardization allowing comparisons of prescribing data from different sources to be made. The costs stated in this report do not represent the true price paid by the NHS on medicines. The estimated costs are used as a proxy for utilization and are not suitable for financial planning.

Data limitations

IMS HPAI data do not link to demographic or to diagnosis information on patients. Therefore, it cannot be used to provide prescribing information on age and sex or for prescribing of specific conditions where the same drug is licensed for more than one indication.