Rivaroxaban for the prevention of venous thromboembolism after total hip or total knee replacement in adults

Issued: April 2009

NICE technology appraisal guidance 170
guidance.nice.org.uk/ta170
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1 Guidance

1.1 Rivaroxaban, within its marketing authorisation, is recommended as an option for the prevention of venous thromboembolism in adults having elective total hip replacement surgery or elective total knee replacement surgery.
2 The technology

2.1 Rivaroxaban (Xarelto, Bayer HealthCare) is an anticoagulant that directly inhibits activated factor X (factor Xa). Inhibiting factor Xa interrupts the pathway of the blood coagulation cascade, inhibiting both thrombin formation and development of thrombi. Rivaroxaban has a marketing authorisation for the prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.

2.2 The summary of product characteristics (SPC) states that rivaroxaban should be taken orally once daily in 10-mg doses. The initial dose should be taken 6–10 hours after surgery, provided that haemostasis has been established. The SPC further states that the duration of treatment depends on the individual risk of the patient for VTE, which is determined by the type of orthopaedic surgery. Recommended treatment durations are 5 weeks for patients having major hip surgery, and 2 weeks for patients having major knee surgery. According to the SPC, approximately 14% of the treated patients across the phase III studies experienced adverse reactions. Bleeding and anaemia occurred in approximately 3.3% and 1% of patients, respectively. Other common adverse reactions were nausea and an increase in transaminases. The SPC states that the risk of bleeding may be increased in certain patient groups, for example those with uncontrolled severe arterial hypertension and/or those taking other treatments that affect haemostasis. For full details of side effects and contraindications, see the SPC.

2.3 Rivaroxaban costs £45.00 for a pack of ten 10-mg tablets (£135.00 for 30 tablets), excluding VAT (NHS list price as reported by the manufacturer). The cost of treatment is estimated to be £63.00 (based on 14 tablets over 2 weeks) for knee replacement surgery and £157.50 for hip replacement surgery (based on 35 tablets over 5 weeks). Costs may vary in different settings because of negotiated procurement discounts.
3 The manufacturer's submission

The Appraisal Committee (appendix A) considered evidence submitted by the manufacturer of rivaroxaban and a review of this submission by the Evidence Review Group (ERG; appendix B).

3.1 The manufacturer's submission compared rivaroxaban with enoxaparin, a low molecular weight heparin (LMWH), using direct evidence from randomised controlled trials (RCTs), and with dabigatran, using RCT evidence in a mixed-treatment comparison. Outcomes analysed included: incidence of deep vein thrombosis (DVT); incidence of pulmonary embolism (PE); mortality; adverse effects of treatment including bleeding events; post-DVT complications including post-thrombotic syndrome; length of hospital stay; and health-related quality of life. The manufacturer's submission did not include analysis of outcomes at the site of the orthopaedic intervention, such as joint infection. There was no comparison with fondaparinux.

3.2 The manufacturer conducted a systematic review that identified six RCTs comparing rivaroxaban with other therapies for the prevention of VTE. Four RCTs met the inclusion criteria (RCTs involving patients aged 18 years or older having hip or knee replacement, comparing rivaroxaban with other therapies including placebo): RECORD 1 and RECORD 2 recruited people having total hip replacement surgery and RECORD 3 and RECORD 4 recruited people having total knee replacement surgery. The other two trials were excluded because they were phase II, dose-ranging studies. The primary endpoint for all four included trials was a composite comprising any DVT, non-fatal PE and death from all causes.

3.3 The RECORD 1 (n = 4541) and RECORD 2 (n = 2509) trials were multicentre, prospective, double-blind, parallel-group design RCTs comparing rivaroxaban with enoxaparin for the prevention of VTE after total hip replacement surgery. In RECORD 1, rivaroxaban was administered at a dosage of 10 mg once daily for 35 days starting on the day of surgery. Enoxaparin was administered at a dosage of 40 mg starting 1 day before surgery and for 35 days thereafter. For this study, the manufacturer reported a statistically significant difference in the incidence of the composite primary endpoint between rivaroxaban and enoxaparin based on a 'modified' intention to treat (MITT) analysis. The
primary endpoint occurred in 1.1% of the rivaroxaban group compared with 3.7% of the enoxaparin group; relative risk reduction (RRR) was 70% (95% confidence interval [CI] 49 to 82, \( p < 0.001 \)). The manufacturer further reported the results of the secondary endpoint: major VTE (a composite of proximal DVT, non-fatal PE and VTE-related death) for RECORD 1. In this study, in the MITT population, major VTE occurred in 4 (0.2%) patients receiving rivaroxaban compared with 33 (2.0%) patients receiving enoxaparin; the RRR was 88% (95% CI 66 to 96, \( p < 0.001 \)).

3.4 RECORD 2 was a comparison of 35 days of prophylaxis with rivaroxaban 10 mg daily compared with a shorter course (15 days) of enoxaparin prophylaxis at 40 mg daily. The manufacturer reported a statistically significant difference in the incidence of the composite primary endpoint between rivaroxaban and enoxaparin in the MITT analysis; 2.0% in the rivaroxaban group compared with 9.3% in the enoxaparin group (RRR 79%, 95% CI 65 to 87). The secondary endpoint, major VTE, occurred in 6 (0.6%) patients receiving rivaroxaban compared with 49 (5.1%) patients receiving enoxaparin (\( p < 0.0001 \)).

3.5 The RECORD 3 (\( n = 2531 \)) and RECORD 4 (\( n = 3148 \)) trials were multicentre, prospective, double-blind, parallel-group design RCTs comparing rivaroxaban with enoxaparin for the prevention of VTE after total knee replacement surgery. In both RECORD 3 and RECORD 4 rivaroxaban was administered at a dosage of 10 mg once daily for 10–14 days starting on the day of surgery. In RECORD 3 the comparator was enoxaparin at a dosage of 40 mg once daily, starting the day before surgery and for 10–14 days thereafter. The MITT analysis showed a statistically significant difference in the incidence of the composite primary endpoint: 9.6% in the rivaroxaban group compared with 18.9% in the enoxaparin group (RRR 49%, 95% CI 35 to 61). Major VTE occurred in 9 (1.0%) patients receiving rivaroxaban compared with 24 (2.6%) patients receiving enoxaparin (RRR 62%, 95% CI 18 to 82; \( p = 0.02 \)).

3.6 In RECORD 4 the comparator was enoxaparin at a higher dosage of 30 mg twice daily starting 1 day before surgery and continuing for 10–14 days thereafter. In this study, the composite primary outcome occurred in 6.9% and 10.1% of the rivaroxaban and enoxaparin groups, respectively (\( p < 0.012 \)).
RECORD 4 found a lower incidence of major VTE in patients treated with rivaroxaban compared with enoxaparin.

3.7 The manufacturer used the per protocol population to test for non-inferiority of rivaroxaban compared with enoxaparin. The MITT analysis was used as supportive analysis in the test for superiority of rivaroxaban over enoxaparin. The manufacturer presented a range of meta-analyses that pooled the RECORD 1 and RECORD 2 studies for total hip replacement and the RECORD 3 and RECORD 4 studies for total knee replacement. Because of a lack of head-to-head trials between rivaroxaban and dabigatran, the manufacturer used an indirect comparison methodology that compared rivaroxaban and dabigatran, with enoxaparin as the common comparator. The analysis compared the incremental effect of rivaroxaban over enoxaparin to the incremental effect of dabigatran over enoxaparin. The comparison of these incremental effects allowed the indirect estimation of the incremental effect of rivaroxaban over dabigatran. The manufacturer stated that the indirect comparison methods used in this analysis were widely published and ensured that randomisation from the original trials was preserved. The results of these analyses were submitted to NICE in confidence and are not presented in this document.

3.8 The main safety endpoint in the RECORD trials was the incidence of treatment-emergent major bleeding. The manufacturer reported the rates of major bleeding for patients treated with rivaroxaban and enoxaparin, respectively, as follows. RECORD 1: 0.3% vs 0.1%, p = 0.178; RECORD 2: 0.1% vs 0.1%, p = 0.98; RECORD 3: 0.6% vs 0.5%, p = 0.77; and RECORD 4: 0.7% vs 0.3%, p = 0.11. The incidence of non-major bleeding (comprising clinically relevant non-major bleeding, haemorrhagic wound complications and other non-major bleeding) was similarly low, for rivaroxaban and enoxaparin, respectively, as follows. RECORD 1: 5.8% vs 5.8%; RECORD 2: 6.5% vs 5.5%; RECORD 3: 4.3% vs 4.4%; and RECORD 4: 10.2% vs 9.2%.

3.9 The ERG reviewed the literature search strategy and concluded that it effectively identified literature relevant to the decision problem and used relevant search techniques for systematic review and appraisal. The ERG was satisfied that the RECORD trials were of adequate methodological quality. It
commented that reporting and interpretation of the safety data were good, and concluded that the manufacturer's submission appeared to contain an unbiased estimate of the effectiveness of rivaroxaban in relation to the main comparator, enoxaparin.

3.10 The manufacturer submitted an economic model assessing the cost effectiveness of rivaroxaban compared with enoxaparin in VTE prevention after hip and knee replacement. The model comprised three modules: prophylaxis, post-prophylaxis, and long-term complications. The first two modules represented the acute phase in the form of a decision tree, and the third component represented the chronic phase and was developed as a Markov process. The prophylaxis part of the model was informed by clinical trial events (first 35 days for total hip replacement and 14 days for total knee replacement post-surgery). The post-prophylaxis component reflected the risk of symptomatic VTE events within the first 3 months, and the long-term complications component extrapolated any long-term complications resulting from symptomatic VTE events.

3.11 Key assumptions in the economic evaluation included the assumption that asymptomatic VTE events would not incur any costs and did not have an impact on quality of life. It was assumed that all recurrent VTEs were DVTs. If the clinical trial or indirect comparison did not show a significant difference between the two arms, the probabilities were assumed to be equal in the model. It was also assumed that all PEs in the post-prophylaxis module were non fatal.

3.12 The manufacturer presented base-case analyses based on RECORD 1 and RECORD 2 separately to reflect the different comparator regimens. The base case for the total knee replacement indication did not include an analysis based on RECORD 4 because the higher dosage of 30 mg twice daily for enoxaparin reflected practice in the US rather than the UK. However, the manufacturer presented pooled analysis by total hip replacement, total knee replacement and for all trials together.

3.13 The results showed that rivaroxaban dominated enoxaparin in both total hip replacement (RECORD 1 and 2) and total knee replacement (RECORD 3).
Deterministic sensitivity analysis for RECORD 1 showed that rivaroxaban generally dominated enoxaparin. However with a shorter treatment duration for enoxaparin (but maintaining 35 days’ treatment benefits), the incremental cost-effectiveness ratio (ICER) for rivaroxaban compared with enoxaparin was £14,616 per QALY gained. When the benefits were also adjusted to reflect a reduced duration of prophylaxis, the ICER was £914 per QALY gained. In RECORD 2 the main variable that affected the ICER was excluding long-term complications caused by VTE events. This resulted in an ICER of £58,337 per QALY gained. The manufacturer attributed this change to lower prophylaxis drug costs for enoxaparin compared with rivaroxaban. The treatment duration for rivaroxaban was longer (35 days) compared with enoxaparin (15 days) in this trial, and therefore the prophylaxis drug costs for enoxaparin were lower. The indirect comparison with dabigatran showed that rivaroxaban dominated dabigatran in both total hip replacement and total knee replacement.

3.14 The ERG considered that the approach to the economic modelling was reasonable. However, it noted that some potential events had been excluded from the model. The possibility of further VTE events other than DVT in the longer-term model was not considered and neither was the possibility of intracranial haemorrhage (a health state associated with marked disutility).

3.15 The ERG noted that the conclusions on the cost effectiveness of rivaroxaban were dependent on the assumptions made about parameters that were not statistically significant, and on the appropriateness of pooling data. If all parameters where the p value was greater than 0.05 were set equivalent for rivaroxaban and the comparator, then assuming that all trials were pooled, rivaroxaban dominated the comparators. When the observed data were used and total hip replacement and total knee replacement were pooled separately, rivaroxaban did not always dominate enoxaparin and dabigatran in the total knee replacement indication. The ERG considered it more appropriate to model with observed data than by setting parameters to be equivalent when there was no statistically significant difference. The ERG also considered that pooling the data from all trials was reasonable in the circumstances. However, accepting these points, the differences in costs and QALYs gained across all analyses were extremely small.
3.16 Full details of all the evidence are in the manufacturer's submission and the ERG report.
4 Consideration of the evidence

4.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of rivaroxaban for the prevention of VTE after elective total hip or knee replacement surgery in adults having considered evidence on the nature of the condition and the value placed on the benefits of rivaroxaban by people with experience of VTE, those who represent them, and clinical specialists. It was also mindful of the need to take account of the effective use of NHS resources.

4.2 The Committee discussed the decision problem framework and in particular the major outcomes that were considered. The Committee was concerned that joint outcomes had not been included in the decision problem. It noted, however, that the main trials for total hip and total knee replacement did not evaluate joint outcomes. The Committee also noted that fondaparinux was not included in the manufacturer's decision problem, although the NICE clinical guideline 'Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in inpatients undergoing surgery' (NICE clinical guideline 46 [Replaced by NICE clinical guideline 92]) recommended that in addition to mechanical prophylaxis, people at increased risk of VTE and people undergoing orthopaedic surgery should be offered LMWH. The guideline also recommended that fondaparinux, within its licensed indications, may be used as an alternative to LMWH. The Committee noted that the manufacturer had not included fondaparinux as a comparator because it was used in less than 2% of patients in current UK clinical practice. The Committee noted comments from clinical specialists that drugs for the prevention of VTE are not routinely used by all orthopaedic surgeons because of concerns that they may increase the incidence, or worsen the consequences, of wound haemorrhage in the site of the orthopaedic surgery.

4.3 The Committee discussed the clinical effectiveness of rivaroxaban compared with enoxaparin and dabigatran in people having elective hip or knee surgery. It noted the direct RCT evidence of a comparison of rivaroxaban and enoxaparin, and the indirect comparison of rivaroxaban versus dabigatran. The Committee agreed that the methodology used in the indirect comparison was
plausible and therefore it was reasonable to consider the results of this comparison.

4.4 The Committee considered evidence on the clinical effectiveness of rivaroxaban compared with enoxaparin. It discussed the applicability of the trials to UK clinical practice, noting that there is variation in prevention strategies. The Committee discussed the relevance of the RECORD 1, 2 and 3 trials, in which the patients in the control arm received 40 mg enoxaparin once daily, and agreed that the data from these trials were applicable to UK clinical practice. The Committee noted that the RECORD 4 study used an alternative dosing regimen of 30 mg enoxaparin twice daily that did not reflect the UK clinical setting, but agreed that the results of this study contributed to the overall evidence base and so were relevant for consideration. The Committee discussed the outcome data from these trials and was concerned about the use of surrogate outcomes as valid predictors of clinically relevant outcomes. Clinical specialists indicated that a major component of the composite primary outcome of the studies (DVT detected by venogram) was a surrogate outcome that was objectively assessed and allowed comparison between prevention strategies. Furthermore, the clinical specialists indicated that there was a direct relationship between venographically assessed outcomes and symptomatic outcomes. The Committee noted that the Guideline Development Group of NICE clinical guideline 46 had accepted venographically determined outcomes after careful consideration.

4.5 The Committee discussed the results of the RECORD studies and concluded that rivaroxaban was at least as effective as enoxaparin in preventing VTE. The Committee considered adverse events such as bleeding, noting that the relative risk of major bleeding numerically favoured enoxaparin. The Committee noted that the chosen dose of rivaroxaban appeared to increase efficacy in prevention of VTE after surgery, with a small increase in risk of major bleeding when compared with enoxaparin. It concluded that rivaroxaban at its licensed dosage of 10 mg daily might be more efficacious than enoxaparin in preventing VTE but this was accompanied by a small increased risk of major bleeding. The Committee was persuaded by testimony from the clinical specialists that there was a ‘trade off’ to be made between increasing anticoagulant efficacy and the risk of adverse effects, including major bleeding.
4.6 The Committee considered evidence on the clinical effectiveness of rivaroxaban compared indirectly with dabigatran that showed that rivaroxaban significantly reduced the relative risk of the major primary endpoints. However, the Committee noted that in this analysis the relative risk of major bleeding favoured dabigatran although this difference was not statistically significant. It agreed that on balance, rivaroxaban and dabigatran had broadly similar efficacy profiles, and noted the need to balance prevention of VTE with possible adverse effects, particularly the incidence of major bleeding events.

4.7 The Committee discussed the benefits to patients of treatments given orally compared with subcutaneous injection. The Committee heard from the clinical specialists and patient experts that in general, oral dosing was preferred to subcutaneous injection. It discussed the implications of providing an option for oral administration in adherence to treatment. The Committee discussed whether a recommendation for an oral treatment rather than a subcutaneous injection would give rise to any issues related to equalities and diversity legislation. The Committee concluded that there were no issues related to equality of access to treatment that it would need to take into account when considering positively recommending rivaroxaban. The Committee also agreed that the option of oral treatment would be preferred by some patients and their clinicians.

4.8 The Committee discussed the evidence submitted by the manufacturer on the cost effectiveness of rivaroxaban for the prevention of VTE in people having total hip or total knee replacement, the ERG's critique of the manufacturer's submission, and the manufacturer's response to the clarification requested by the ERG. The base-case analysis in the manufacturer's submission showed that rivaroxaban dominated enoxaparin and dabigatran in both total hip and total knee replacement. The Committee noted that this base-case analysis depended on the exclusion of the numerically increased adverse events for rivaroxaban compared with enoxaparin on the basis that they were not statistically significant. The Committee was concerned that this might not be in line with normal economic modelling procedures and took into account the ERG's preference for using observed data in the analysis. The Committee noted that the main variables that affected the output of the model were the
rate of fatal PE and whether the model used observed values from the trials when there were insignificant differences in outcomes.

4.9 The ERG’s exploratory analysis showed that rivaroxaban did not always dominate enoxaparin and dabigatran in total knee replacement when the observed values from the trials were used. The Committee also noted the ERG’s comments that the model did not incorporate the effect of fatal PE but concluded that there were very small differences in the costs and QALYs in any of the analyses presented.

4.10 The Committee noted that although the primary clinical outcome data indicated that rivaroxaban was superior to enoxaparin and dabigatran, several of the point estimates in the economic analysis favoured enoxaparin. It also noted that the relative risk for major bleeding was in favour of enoxaparin and dabigatran. The Committee was mindful that the differences in the effectiveness and cost data were very small and therefore the ICERs were very sensitive to minor changes in assumptions. The Committee acknowledged that oral administration of rivaroxaban without the need for haematological monitoring would reduce administration costs and may support adherence to treatment.

4.11 The Committee concluded that, on balance, rivaroxaban, enoxaparin and dabigatran had very similar costs and benefits in the prevention of VTE. Therefore, the Committee agreed that the use of rivaroxaban for the prevention of VTE is an appropriate use of NHS resources and that rivaroxaban should be recommended as an option for the prevention of venous thromboembolism in adults having elective total hip replacement surgery or elective total knee replacement surgery.
5 Implementation

5.1 The Secretary of State and the Welsh Assembly Minister for Health and Social Services have issued directions to the NHS on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends use of a drug or treatment, or other technology, the NHS must provide funding and resources for it within 3 months of the guidance being published. If the Department of Health issues a variation to the 3-month funding direction, details will be available on the NICE website. The NHS is not required to fund treatments that are not recommended by NICE.

5.2 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraph above. This means that, if a patient is having elective total hip replacement surgery or elective total knee replacement surgery and the doctor responsible for their care thinks that rivaroxaban is the right treatment for preventing venous thromboembolism, it should be available for use, in line with NICE’s recommendations.

5.3 NICE has developed tools to help organisations implement this guidance (listed below).

- A costing statement explaining the resource impact of this guidance.
- Audit support for monitoring local practice.
6 Recommendations for further research

6.1 Further head-to-head trials of rivaroxaban compared with enoxaparin and dabigatran in both total hip replacement and total knee replacement would be useful to strengthen the evidence base for this comparison.
7 Related NICE guidance


- Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in inpatients undergoing surgery. NICE clinical guideline 46 (2007). [Replaced by NICE clinical guideline 92]
8 Review of guidance

8.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider whether the technology should be reviewed. This decision will be taken in the light of information gathered by the Institute, and in consultation with consultees and commentators.

8.2 The guidance on this technology was considered for review in February 2012. Details are on the NICE website.

Andrew Dillon
Chief Executive
April 2009
Appendix A: Appraisal Committee members, guideline representatives and NICE project team

A Appraisal Committee members

The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets three times a month except in December, when there are no meetings. The Committee membership is split into three branches, each with a chair and vice chair. Each branch considers its own list of technologies, and ongoing topics are not moved between the branches.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Professor David Barnett (Chair)
Professor of Clinical Pharmacology, University of Leicester

Professor Philip Home (Vice Chair)
Professor of Diabetes Medicine, Newcastle University

Dr Amanda Adler
Consultant Physician, Cambridge University Hospitals Trust

Professor A E Ades
MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol

Dr Tom Aslan
General Practitioner, Stockwell, London
The following individual, representing the Guideline Development Group responsible for developing the Institute's clinical guideline related to this topic, was invited to attend the meeting to observe and to contribute as an adviser to the Committee:

- Ms Karen Head, Project Manager, National Collaborating Centre for Acute Care

C NICE project team

Each technology appraisal is assigned to a team consisting of one or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

David Chandiwana
Technical Lead

Janet Robertson
Technical Adviser

Bijal Chandarana
Project Manager
Appendix B: Sources of evidence considered by the Committee

A. The Evidence Review Group (ERG) report for this appraisal was prepared by the School of Health and Related Research (ScHARR), University of Sheffield:


B. The following organisations accepted the invitation to participate in this appraisal. They were invited to comment on the draft scope. Organisations listed in I were also invited to make written submissions. Organisations listed in II and III gave their expert views on rivaroxaban by providing a written statement to the Committee. Organisations listed in I, II and III have the opportunity to appeal against the final appraisal determination.

I) Manufacturer/sponsor:

- Bayer HealthCare (rivaroxaban)

II) Professional/specialist and patient/carer groups:

- Anticoagulation Europe
- British Association for Surgery of the Knee
- British Orthopaedic Association
- British Society for Haematology
- British Society for Haemostasis and Thrombosis
- British Thoracic Society
- DVT Awareness Campaign
- Lifeblood: The Thrombosis Charity
- Royal College of Nursing
- Royal College of Pathologists
III) Other consultees:

- Department of Health
- Welsh Assembly Government

IV) Commentator organisations (did not provide written evidence and without the right of appeal):

- British National Formulary
- Department of Health, Social Services and Public Safety for Northern Ireland
- GlaxoSmithKline (fondaparinux sodium)
- Leo Laboratories (tinzaparin sodium)
- National Collaborating Centre for Acute Care
- National Institute for Health Research (NIHR) Health Technology Assessment Programme (HTA Programme)
- Pfizer Ltd (dalteparin sodium)
- Research Institute for the Care of the Elderly
- Sanofi-Aventis Ltd (enoxaparin sodium)
- School of Health and Related Research (ScHARR), University of Sheffield

C. The following individuals were selected from clinical specialist and patient advocate nominations from the non-manufacturer/sponsor consultees and commentators. They gave their expert personal view on rivaroxaban by providing oral evidence to the Committee:

- Annya Stephens – Boal, Executive Officer, nominated by Lifeblood: The Thrombosis Charity – patient expert
- Eve Knight, Chief Executive, nominated by AntiCoagulation Europe – patient expert
- Colin Howie, Consultant Orthopaedic Surgeon, nominated by the British Orthopaedic Association – clinical specialist
• Professor Mike Laffan, Professor of Haemostasis and Thrombosis, nominated by the British Society for Haematology – clinical specialist
Changes after publication

**February 2014:** implementation section updated to clarify that rivaroxaban is recommended as an option for preventing venous thromboembolism after total hip or total knee replacement in adults. Additional minor maintenance update also carried out.

**March 2012:** minor maintenance
About this guidance

NICE technology appraisal guidance is about the use of new and existing medicines and treatments in the NHS in England and Wales.

This guidance was developed using the NICE single technology appraisal process.

The recommendations from this guideline have been incorporated into a NICE Pathway. We have produced a summary of this guidance for patients and carers. Tools to help you put the guidance into practice and information about the evidence it is based on are also available.

Your responsibility

This guidance represents the views of NICE and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

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