NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Apixaban for the prevention of venous thromboembolism in people undergoing elective knee and hip replacement surgery

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Dr Raza Alikhan

Name of your organisation:

British Society of Haematology

And

Royal College of Pathologists

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? √
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? √
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?
- other? (please specify)

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What is the expected place of the technology in current practice?

Patients undergoing orthopaedic surgery (hip and knee replacement) without thromboprophylaxis are at high risk of DVT. There are a number of complications associated with DVT, including acute pulmonary embolism and long-term post-thrombotic syndrome. Pulmonary embolism following hip or knee surgery has been shown to be an independent predictor of death [Guijarro et al, Thromb Haemost 2010 105 (4)]

The American College of Chest Physicians (ACCP) guideline: prevention of VTE [Geerts et al. Chest 2008; 381S-454S] is an evidence-based clinical practice guideline in its 8th incarnation; written by a panel of internationally respected experts from North America, Canada and Western Europe. They are the benchmark guidelines in this filed and "recommend that patients undergoing elective THR or TKR receive routine thromboprophylaxis".

The ENDORSE study assessed the number of patients at risk of VTE and determined the use of thromboprophylaxis, using the ACCP guidelines, by evaluating the charts of medical and surgical patients in 32 countries. Worldwide 86% of orthopaedic surgery patients received ACCP-recommended VTE prophylaxis compared to 77.6% of orthopaedic patients in the UK [Kakkar et al. Ann Surg 2010;251:330-338].

NICE CG92 "VTE: reducing the risk" states that all patients admitted to hospital for elective hip or knee replacement surgery should be offered post-operative pharmacological VTE prophylaxis provided that there are no contraindications. Pharmacological prophylaxis includes:
Injectable: low molecular weight heparin (LMWH) (or unfractionated heparin if renal failure), fondaparinux
Oral: dabigatran (NICE TA157) or rivaroxaban (NICE TA170)

The technology (apixaban) is oral and should be initiated in secondary care following elective hip / knee replacement surgery and continued following hospital discharge 32-38 days / 10-14 days respectively. There would be no need for additional professional input.

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The advantages and disadvantages of the technology

In the UK, low molecular weight heparin has been the primary choice for pharmacological thromboprophylaxis in patients undergoing hip or knee surgery. This needs to be administered daily via a subcutaneous injection. In hospital, patients receive this treatment administered daily by a nurse. The risk of VTE persists after discharge from hospital and therefore a district nurse is required to continue to administer thromboprophylaxis or patients are taught to self-inject. This inevitably results in a reduction in treatment compliance due to a lack of district nurse resources and the inconvenience of daily injections. The technology will be easier to administer, will not require district nurse input and should increase patient acceptance and potentially compliance with treatment. There are two alternative oral thromboprophylactic agents that have been approved by NICE for this indication dabigatran (NICE TA157) and rivaroxaban (NICE TA170).

In addition, patients receiving LMWH should have a platelet count measured to test for heparin induced thrombocytopenia (HIT) a rare but potentially devastating complication of heparin based treatment following surgery. Invariably this is not performed following hospital discharge. There is no need for platelet count monitoring with the new technology.

The clinical trial conditions for ADVANCE-2 and -3 reflect those seen in UK practice except that LMWH is usually administered post-operatively in the majority of centres, rather than 12 hours pre-operatively. The use of enoxaparin 30mg twice daily in ADVANCE-1 is not comparable to UK practice and reflects North American practice.

The most important outcome was the primary safety outcome of bleeding. The trial protocol adapted the definitions for bleeding recommended by the International Society of Thrombosis and Haemostasis. In both the knee (ADVANCE-2) and hip (ADVANCE-3) studies there was no increase in the risk of bleeding with the technology when compared to the comparator LMWH (enoxaparin). In addition the technology resulted in a significantly reduced risk of VTE when compared to enoxaparin.

The use of a surrogate outcome, i.e. asymptomatic DVT in clinical trials, assessed by venography is often cited as a reason for not using pharmacological thromboprophylaxis in clinical practice. However, as stated earlier there is an association between DVT and acute PE. A meta-analysis of thromboprophylaxis studies in surgery has shown a 68% reduction in asymptomatic DVT when thromboprophylaxis was compared to placebo. These findings were comparable to a 64% reduction in risk of fatal PE observed in the same analysis [Collins et al N Engl J Med 1988; 318:1162-73].

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Any additional sources of evidence

None

Implementation issues

NICE guidance on this technology has the possibility to increase compliance in the administration of thromboprophylaxis in patients undergoing elective hip and knee replacement surgery.

There would be no need for extra education and training of NHS staff.