Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
www.scottishmedicines.org.uk
Delta House 50 West Nile Street Glasgow G1 2NP Tel 0141 225 6999 Chairman: Professor Jonathan G Fox

edoxaban tosilate 15mg, 30mg, 60mg film-coated tablets (Lixiana®)
SMC No. (1090/15)

Daiichi Sankyo UK Limited

9 October 2015

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in Scotland. The advice is summarised as follows:

ADVICE: following a full submission

edoxaban (Lixiana®) is accepted for use within NHS Scotland.

Indication under review: Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

One phase III study showed non-inferiority of edoxaban versus a vitamin K antagonist for venous thromboembolism recurrence in patients who had received at least five days treatment with low molecular weight heparin or unfractionated heparin. Edoxaban was also associated with a significant reduction in the risk of major and clinically relevant non-major bleeding (composite endpoint).

Chairman,
Scottish Medicines Consortium

Indication

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Dosing Information

Edoxaban 60mg once daily following initial use of parenteral anticoagulant for at least 5 days. Edoxaban and initial parenteral anticoagulant should not be administered simultaneously.

The duration of therapy for treatment of DVT and PE (venous thromboembolism [VTE]), and prevention of recurrent VTE should be individualised after careful assessment of the treatment benefit against the risk for bleeding. Short duration of therapy (at least three months) should be based on transient risk factors (e.g. recent surgery, trauma, immobilisation) and longer durations should be based on permanent risk factors or idiopathic DVT or PE.

Edoxaban 30mg once daily is recommended in patients with one or more of the following clinical factors:

- Moderate or severe renal impairment (creatinine clearance 15 to 50mL/min)
- Low body weight ≤60kg
- Concomitant use of the following P-glycoprotein (P-gp) inhibitors: ciclosporin, dronedarone, erythromycin or ketoconazole

Edoxaban 15mg once daily is only indicated when switching from edoxaban 30mg (in patients with one or more clinical factors for increased exposure) to a vitamin K antagonist together with an appropriate vitamin K antagonist dose.

Product availability date

July 2015

Summary of evidence on comparative efficacy

Edoxaban is a direct factor Xa inhibitor which, in the coagulation cascade, reduces thrombin generation, prolongs clotting time and reduces the risk of thrombus formation. Edoxaban is the third direct factor Xa inhibitor licensed for the treatment of DVT and PE, and prevention of recurrent DVT and PE in adults.[1] Apixaban and rivaroxaban have been accepted for use by SMC for the similar indications, as has dabigatran, a direct thrombin inhibitor.

Evidence of efficacy for the treatment and prevention of VTE comes from the Hokusai-VTE study. This was a phase III, randomised, double-blind, non-inferiority study conducted in patients aged ≥18 years with objectively diagnosed, acute, symptomatic DVT involving the popliteal, femoral, or iliac veins, or acute, symptomatic PE (with or without DVT). Patients were randomised equally (stratified according to the diagnosis [DVT or PE], presence or absence of temporary risk factors, and dose of edoxaban) to edoxaban 60mg orally once daily or warfarin at a dose to maintain the international normalised ratio (INR) between 2.0 and 3.0. All patients received open-label enoxaparin or unfractionated heparin for at least five days, with edoxaban started after the heparin had been stopped and warfarin started at the same time as the heparin. Patients were treated with the oral anticoagulant for 3 to 12 months, depending on the patient's clinical features and preference, as determined by the treating clinician. Edoxaban 30mg daily was used in patients with creatinine clearance of 30 to 50mL/minute or a body

weight of ≤60kg or in patients who were receiving concomitant treatment with potent P-glycoprotein inhibitors.[2,3]

The primary efficacy outcome was the incidence of adjudicated, symptomatic, recurrent VTE, defined as DVT or non-fatal or fatal PE. The overall study period (randomisation to end of 12 months or study closure) was used for the primary analysis and a secondary analysis was conducted in the on-treatment period (the time during which the patients were receiving the study drug or within three days after the study drug was stopped or interrupted). The modified intention-to-treat (mITT) population was used for efficacy analyses and included all patients who underwent randomisation and received at least one dose of study drug. Non-inferiority was concluded if the upper bound of the 95% confidence interval (CI) of the hazard ratio was less than 1.5.[2]

The mean duration of study treatment was 250 days in the edoxaban group and 248 days in the warfarin group. Recurrence of VTE (overall study period) occurred in 3.2% (130/4118) of patients in the edoxaban group and 3.5% (146/4122) of patients in the warfarin group; non-inferiority was concluded. The results of the primary outcome were generally consistent across subgroups. Non-inferiority was also demonstrated for the secondary analysis of VTE recurrence, in the on-treatment period. Results of the primary and secondary analyses of the primary endpoint as well as some secondary endpoints are included in the table below.

Table: primary and some secondary endpoints from the Hokusai-VTE study (mITT population)[2]

	edoxaban* (N=4,118)	**warfarin (N=4,122)**	**Hazard ratio (95% CI) p-value**
Primary endpoint			
Primary analysis: VTE recurrence (overall study period); % (n/N)	3.2% (130/4118)	3.5% (146/4122)	0.89, (0.70 to 1.13) p<0.001 (for non-inferiority)
Secondary analysis: VTE recurrence (on-treatment period); % (n/N)	1.6% (66/4118)	1.9% (80/4122)	0.82, (0.60 to 1.14) p<0.001 (for non-inferiority)
Secondary endpoints			
Recurrent VTE, non-fatal MI, non-fatal stroke, non-fatal systemic embolic event, CV death (overall study period); % (n/N)	2.8% (114/4118)	2.9% (120/4122)	0.95, (0.73 to 1.23) p=0.68
Recurrent VTE, all cause mortality (overall study period); % (n/N)	5.5% (228/4118)	5.5% (228/4122)	1.00, (0.83 to 1.20) p=1.00
Net clinical benefit (VTE plus major bleed) (on-treatment period); % (n/N)	2.9% (120/4118)	3.5% (144/4122)	0.83, (0.65 to 1.06) p=0.14

VTE=venous thromboembolism, MI=myocardial infarction, CV=cardiovascular, CI=confidence interval
*dose of edoxaban was 60mg daily reduced to 30mg in patients with clinical factors as per licensed indication.

Summary of evidence on comparative safety

Any adverse event occurred in a similar proportion of patients in the edoxaban (68% [2821/4118]) and warfarin (71% [2928/4122]) groups, and serious adverse events occurred in 12% (503/4118) versus 13% (544/4122) of patients respectively. Serious adverse events that led to permanent discontinuation of study drug occurred in 2.9% (121/4118) versus 2.5% (105/4122) of patients respectively, and drug-related adverse events that led to permanent discontinuation of study drug occurred in 1.0% (41/4188) and 1.2% (51/4122) of patients respectively. [2]

The principal safety outcome was the incidence of adjudicated clinically relevant bleeding, defined as major and clinically relevant non-major bleeding. Major bleeding was defined as overt, associated with a decrease in haemoglobin ≥2g/dL or requiring a transfusion of ≥2 units of blood, occurring in a critical site, or contributing to death. Clinically relevant non-major bleeding was defined as overt bleeding not meeting the criteria for major bleeding but associated with the need for medical intervention, contact with a physician, or interruption of the study drug or with discomfort or impairment of activities of daily life. The composite endpoint of major and clinically relevant non-major bleeding occurred in a significantly lower proportion of patients in the edoxaban group (8.5% [349/4118]) than in the warfarin group (10% [423/4122]); hazard ratio 0.81 (95% CI: 0.71 to 0.94), p=0.004 (for superiority). The risk difference was -1.8% (95% CI: -3.04% to -0.53%). There was no significant difference between groups for major bleeding: 1.4% (56/4118) versus 1.6% (66/4122) of patients in the edoxaban group and warfarin groups respectively (hazard ratio 0.84 [95% CI: 0.59 to 1.21]). [2]

The proportions of patients requiring hospitalisation for major bleeding (1.2% versus 1.2%), transfusion ≥2 units (0.7% versus 0.5%), need for surgery (<0.1% versus <0.1%) and hospitalisation with intensive care unit (0.3% versus 0.4%) were similar between edoxaban and warfarin groups.[3]

Summary of clinical effectiveness issues

Edoxaban is the third direct factor Xa inhibitor licensed for the treatment of DVT and PE, and prevention of recurrent DVT and PE in adults. Apixaban and rivaroxaban have been accepted for use by SMC for similar indications. In addition, dabigatran, a direct thrombin inhibitor, has also been accepted for use by SMC. Current Scottish guidance, which predates the availability of the direct oral anti-coagulants for this indication, is to use a vitamin K antagonist for at least three months after a first episode of limb DVT or PE.[4] Clinical experts consulted by SMC reported the use of rivaroxaban, apixaban and dabigatran for the indication under review, with some use of warfarin in specific patient groups.

In the phase III pivotal study, the non-inferiority of edoxaban versus warfarin was concluded in a patient population with an index event of DVT only (60%), PE only (30%) and PE with DVT (10%). The treatment effect was consistent in patients with DVT only and in patients with PE with or without DVT. The European Medicines Agency (EMA) noted that the non-inferiority margin of 1.5 was restrictive, when compared to recent studies with novel oral anti-coagulants for the treatment of VTE,that used margins of 1.80 to 2.75.[3]

While the treatment duration was determined by the treating clinician (mirroring clinical practice) and could range from 3 to 12 months, the EMA noted that a second randomisation or a second study in patients having received anticoagulation after three to six months, would have been preferred, so that randomised clinical data versus placebo or active comparator for extended treatment of VTE would be available. However, the EMA also noted that the study allowed a comparison with warfarin (rather

than placebo) up to 12 months which provided a more robust comparison as to the real world risk-benefit of continued treatment.[3]

In both groups, there was a large difference in VTE events between the overall study period analysis and the on-treatment period analysis, indicating that about half the events during the overall study period occurred after anticoagulation had been stopped. This provides reassurance that there was no difference in rebound VTE between groups. However, these data suggest that longer treatment durations for many patients would have been beneficial and, indeed, the optimal treatment duration with edoxaban is unclear from the study.[2,3] The summary of product characteristics states that treatment duration should be individualised taking into consideration treatment benefit and the risk for bleeding, and does not include advice on maximum duration of treatment.[1]

The Committee for Medicinal Products for Human Use (CHMP) considered that the primary analysis of the primary endpoint should have focused on the per protocol (PP) population in the on-treatment period, as well as the mITT analysis for the overall study period. The PP analysis was undertaken as sensitivity analysis only, and also demonstrated non-inferiority of edoxaban with warfarin.[3]

Patients in the warfarin group received at least monthly monitoring of their INR whilst on study, which resulted in an overall time in therapeutic range of 64%, which in consistent with a recently published meta-analysis of studies of vitamin K antagonists in the treatment of DVT.[2,5]

There are no direct comparative data for edoxaban versus the other novel oral anti-coagulants. A network meta-analysis (NMA) using fixed effects and including six studies, was performed to estimate the relative effects of edoxaban, warfarin, apixaban, dabigatran and rivaroxaban. The outcomes assessed were VTE recurrence, composite of major and clinically relevant non-major bleeding, major bleeding, clinically relevant non-major bleeding, VTE related death, and net clinical benefit (reported in three studies, composite of VTE recurrence and major bleeding). The NMA demonstrated that edoxaban had a similar efficacy profile (VTE recurrence) to all comparators and generally most outcomes in the NMA were similar across the comparators. Edoxaban had a lower risk of clinically relevant non-major bleeding compared with rivaroxaban and warfarin. Edoxaban had a higher risk of major bleeding and clinically relevant non-major bleeding when compared with apixaban, and a greater risk of clinically relevant non-major bleeding when compared with dabigatran. The NMA is limited by heterogeneity in study design, including blinding and variation in the duration of treatment across the studies.

There is no specific antidote to edoxaban since it acts at a different step in the coagulation cascade from warfarin and the standard strategies used to reverse warfarin are not appropriate. Edoxaban dose interruption or discontinuation and symptomatic treatment are initially recommended in patients who bleed. This may also be an issue in patients who require emergency surgery. The SPC advises that edoxaban should be stopped at least 24 hours before surgical or other procedures.[1] For life-threatening bleeding that cannot be controlled with transfusion or haemostasis, the administration of a 4-factor prothrombin complex concentrate has been shown to reverse the effects of edoxaban 30 minutes after completing the infusion.[1]

Use of edoxaban and dabigatran require that heparin is administered for ≥5 days and 5 days (respectively) then discontinued before edoxaban and dabigatran are commenced.[1,6] This contrasts with rivaroxaban and apixaban which do not require to be administered after heparin.[7,8] Edoxaban, like rivaroxaban (after the first 3 weeks), offers once daily dosing, while dabigatran and apixaban are administered twice daily.

Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis which compared edoxaban with warfarin, rivaroxaban, dabigatran and apixaban in the licensed population. The company has also indicated that treatment with warfarin, dabigatran and edoxaban was preceded by treatment with low molecular weight heparin (LMWH), and that patients with active cancer were excluded from the analysis.

The company used a Markov model consisting of 11 health states, which represented both the treatment and clinical events associated with the management and complications of VTE. In terms of model structure, patients entered the model in the on-treatment state and could discontinue treatment following an adverse event or after completing 12 months of treatment. Patients who were receiving treatment could transition to the major bleed (MB), clinically relevant non major bleed (CRNMB), heparin induced thrombocytopenia (HIT; if treated with heparin), chronic thrombocytopenia pulmonary hypertension (CTEPH), or stroke health states. Post-thrombotic syndrome (PTS) was included in the model; however, it was not modelled as a health state but as a complication that impacted upon cost and quality of life. Patients who were on and off treatment were also at risk of recurrent VTE events.

The main sources of clinical data used in the analysis were the Hokusai-VTE study and an NMA. The Hokusai-VTE study was primarily used to generate estimates for warfarin in relation to key clinical variables, while the NMA provided odds ratios for edoxaban, dabigatran, rivaroxaban and apixaban compared to warfarin in relation to experiencing VTE recurrence, CRNM and MB. The published literature was used in the economic model in the absence of data from the Hokusai-VTE study.

The company selected utility values from published sources, and patients were assigned utilities according to their health state. Baseline utility was also adjusted in the economic model depending on the age of the patient.

Medicines acquisition costs were included in the analysis, as were the costs associated with administration of the LMWH and monitoring of warfarin. The economic model assumed that patients treated with warfarin would require 9 INR monitoring visits in the first 3 months then 5 visits per quarter. The economic model assumed that patients treated with apixaban, rivaroxaban and dabigatran did not require monitoring. The costs of managing and treating the disease and adverse events were also included in the analysis.

The base case results were presented as a fully incremental analysis which considered edoxaban, apixaban, dabigatran, rivaroxaban and warfarin. The result indicated that edoxaban was dominant (i.e. more effective and less costly) compared to warfarin and dabigatran. However, edoxaban was dominated by apixaban and rivaroxaban. Apixaban also dominated all other treatments in the analysis. The company also presented the base case result in terms of pairwise comparisons of edoxaban versus apixaban, dabigatran, rivaroxaban and warfarin respectively. The conclusions of these analyses reflected the incremental analysis described above.

The company provided scenario analyses which removed results from the NMA which were not statistically significant. In these, edoxaban remained dominant versus warfarin, dominated by apixaban and rivaroxaban and edoxaban was less effective and less costly compared to dabigatran. If lifelong treatment duration was used in the analysis, edoxaban remained dominant versus warfarin, dominated by rivaroxaban and was less effective and less costly versus apixaban and dabigatran respectively. If a 3 or 6 month treatment duration was used in the analysis, the same conclusions

were reported as in the base case. A scenario analysis which used values for edoxaban based on the pivotal study and not the NMA reported that edoxaban remained dominant versus warfarin.

The company also reported deterministic one way sensitivity analysis for edoxaban versus warfarin, dabigatran, apixaban and rivaroxaban respectively. In most cases, the conclusions were consistent with the base case analyses. However, for the comparison against warfarin, the analysis was most sensitive to increasing odds ratio for VTE recurrence after 3 months for edoxaban (£8,770,661) increasing the probability of VTE recurrence between 3 and 12 months for warfarin (£2,356,791), reducing the probability of VTE recurrence after 12 months for warfarin (£803,069) and reducing the probability of CTEPH between 3 and 12 months for warfarin (£373,459). For the comparison versus dabigatran the analysis was most sensitive to increasing the odds ratio for VTE recurrence between 14 days and 3 months for edoxaban (£97,990).

The main weaknesses were:

- The analysis indicated that edoxaban was not cost-effective against all comparators; rivaroxaban and apixaban both dominated edoxaban in the base case analysis and when non-significant differences were excluded from the economic model in a sensitivity analysis. However, the submitting company stated that in terms of costs and QALYs there was little difference between the medicines. For example, in the base case analysis, edoxaban was 0.0131 and 0.0088 QALYs less effective than apixaban and rivaroxaban respectively and in terms of costs, edoxaban was around £105 and around £73 more expensive than apixaban and rivaroxaban over the duration of the analysis. As noted above, while SMC experts indicate that rivaroxaban, apixaban and dabigatran are used in practice, warfarin is still a treatment option for some patients and the analysis demonstrated cost-effectiveness against warfarin.
- There was some uncertainty related to changes in the assumptions surrounding the number and cost of INR monitoring visits for patients treated with warfarin. Assuming 6 INR visits in the first 3 months followed by 3 visits every quarter, edoxaban remained dominant versus warfarin, but when this frequency of visits was combined with reduced costs of a visit (from £56 in the base case to £25 or £30), the ICERs rose dramatically. However, as with the previous weakness, it is noted that the large ICERs generated by the sensitivity analysis may be a product of very small differences in incremental costs and QALYs.

Despite these weaknesses the economic case has been demonstrated.

Summary of patient and public involvement

The following information reflects the views of the specified Patient Groups.

- Submissions were received from AntiCoagulation Europe (ACE) and Thrombosis UK, which are both registered charities.

- Both AntiCoagulation Europe and Thrombosis UK have received pharmaceutical company funding in the past two years, but neither has received funding from the submitting company.

- Experiencing a DVT and a PE for the first time can be devastating. Both DVT and PE are serious conditions that require urgent investigation and immediate treatment with anticoagulants for periods up to six months or sometimes long term to prevent risk of recurrence. A subsequent recurrence of VTE can cause distress, worsening health problems, hospitalisation and impact on work, travel and day to day living.

- Many of these patients will be on warfarin which requires regular INR monitoring and can be affected by diet and other medications. Patients can find it difficult to get time off work to attend frequent clinic appointments. Edoxaban has a simple once daily dosage and would usually only need one blood test a year to check renal function.

- Edoxaban is an oral medicine, does not require regular INR monitoring and has fewer interactions with other medicines, over the counter treatments and complementary treatments than warfarin. Therefore, there would be fewer adjustments required to diet and lifestyle. This would impact positively on patients' day to day, social and working lives.

Additional information: guidelines and protocols

The Scottish Intercollegiate Guideline Network (SIGN) published national clinical guideline 122; prevention and management of venous thromboembolism, in December 2010.[4] SIGN advises that heparin, LMWH or unfractionated (UFH) or fondaparinux are appropriate agents for the initial treatment of a patient presenting with PE. In confirmed PE, treatment should be continued for at least five days and until the INR is ≥2. Heparin/fondaparinux therapy can then be discontinued in the majority of patients who are not at high risk of recurrent PE. It is recommended that patients presenting with a suspected DVT should be treated with LMWH or fondaparinux until diagnosis is confirmed. Where a DVT is confirmed, patients should continue on LMWH or fondaparinux for at least five days and until the INR is ≥2. Intravenous UFH may be used as an alternative treatment in certain patients e.g. bleeding risk is high or imminent thrombolysis. SIGN recommends that treatment with a vitamin K antagonist (VKA) should be initiated after a first episode of PE or DVT. LMWH may be used as an alternative where VKA therapy is unsuitable. Treatment should aim to achieve a target INR of ≥2.5. VKA treatment should be sustained for at least 3 months.

The National Institute for Health and Care Excellence (NICE) published a clinical guideline 144; venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing, in June 2012.[9] NICE recommends a choice of LMWH or fondaparinux for the acute treatment of confirmed PE or DVT. UFH should be used as alternative for patients with severe renal impairment, an increased risk of bleeding or PE with haemodynamic instability. Treatment should be continued for at least five days or until an INR of ≥2 has been sustained for at least 24 hours. In patients with confirmed proximal DVT or PE, offer VKA within 24 hours of diagnosis and continue for three months. In patients with an unprovoked PE or DVT, VKA therapy may be offered beyond three months. Individual patient bleeding risk and risk of VTE recurrence should be taken into consideration when planning treatment.

The above guidelines predate the availability of the direct oral anti-coagulants for this indication.

The NICE clinical pathway for the treatment of VTE notes that apixaban, dabigatran etexilate and rivaroxaban are all recommended as options for the treatment and prevention of deep vein thrombosis and pulmonary embolism in adults.[10]

Additional information: comparators

Apixaban, dabigatran, rivaroxaban, LMWH and warfarin.

Cost of relevant comparators

Drug	Dose Regimen	Cost per 6 months treatment (£)
edoxaban*	**30 to 60mg orally once daily**	**382**
rivaroxaban	15mg orally twice daily for 21 days then 15 to 20mg orally once daily	426
apixaban	*Treatment:* 10mg twice daily for 7 days then 5mg twice daily *Prevention*: 2.5mg twice daily	*Treatment (6 months)*: 415 *Prevention (6 months)*: 400
dabigatran*	110 to 150mg orally twice daily	403
warfarin	As determined by prothrombin time**	6

		Cost for 5 days treatment (£)
dalteparin	15,000 units once daily by subcutaneous injection	42
enoxaparin	1.5mg/kg every 24 hours by subcutaneous injection	40

*cost excludes the 5 days heparin treatment required before edoxaban and dabigatran are commenced.
**Average daily dose of warfarin assumed to be 5mg.
Doses are for general comparison and do not imply therapeutic equivalence. Costs from eVadis on 24 July 2015 and MIMS (for edoxaban). Dose of enoxaparin (100mg) and dose of dalteparin (15,000 units, dose-banded) based on 70kg adult.

Additional information: budget impact

The company estimated that 5,905 patients in year 1 would be eligible for treatment, rising to 6,285 patients in year 5. The market share estimated by the company was 0.05% in year 1, rising to 7.42% in year 5. When market share was taken into account, the company estimated 3 patients would be treated in year 1 rising to 466 in year 5.

The company estimated the gross medicines budget impact to be £2k in year 1, rising to £350k in year 5. As medicines were assumed to be displaced, the net medicines budget impact was estimated as savings of £160 in year 1, rising to £26k in year 5. These figures assumed a 12 month treatment duration and displacement largely of rivaroxaban.

References

The undernoted references were supplied with the submission. Those shaded in grey are additional to those supplied with the submission.

1. Edoxaban film-coated tablets (Lixiana®) Summary of product characteristics. Daiichi Sankyo UK Limited. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated June 2015.

2. Buller HR, Decousus H, Grosso MA, et al. Edoxaban versus warfarin for the treatment of symptomatic venous thromboembolism. N Engl J Med 2013; 369(15):1406-1415

3. European Medicines Agency. European public assessment report for edoxaban (Lixiana). EMA/321083/2015 23 April 2015.

4. Scottish Intercollegiate Guidelines Network (SIGN). National clinical guideline 122; prevention and management of venous thromboembolism. December 2010.

5. Erkens P, ten Cate H, Buller H. Benchmark for time in therapeutic range in venous thromboembolism: a systematic review and meta-analysis. PLoS ONE 7(9): e42269. doi:10.1371/journal.pone.0042269

6. Rivaroxaban film-coated tablets (Xarelto®) Summary of product characteristics. Bayer plc. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated July 2015.

7. Apixaban film-coated tablets (Eliquis®) Summary of product characteristics. Bristol-Myers Squibb-Pfizer Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated July 2014.

8. Dabigatran hard capsules (Pradaxa®) Summary of product characteristics. Boehringer Ingelheim Limited. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated December 2014.

9. National Institute for Health and Care Excellence (NICE). Clinical guideline 144; Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing. June 2012

10. National Institute for Health and Care Excellence (NICE). Treating venous thromboembolism. NICE pathway. 2015.

This assessment is based on data submitted by the applicant company up to and including 11 September 2015.

Drug prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.