Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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dabigatran etexilate, 110mg, 150mg capsules (Pradaxa®) SMC No. (995/14)
Boehringer Ingelheim Ltd.

05 September 2014

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

dabigatran etexilate (Pradaxa®) 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.

Dabigatran etexilate was non-inferior to a vitamin K antagonist for recurrent symptomatic venous thromboembolism events (VTE) and death related to VTE in three phase III studies (two in the treatment of DVT/PE and one in the prevention of recurrent DVT/PE).

The economic case was based on evidence relating to a maximum of 18 months treatment so the cost-effectiveness of longer term use is uncertain.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

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Indication

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

Dosing Information

Dabigatran etexilate 150mg capsule twice daily following treatment with a parenteral anticoagulant for at least 5 days. The duration of therapy should be individualised after careful assessment of the treatment benefit against the risk for bleeding. Short duration of therapy (at least 3 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.

A dose of 110mg twice daily may be used in certain patient groups; refer to the summary of product characteristics for further detail.

Product availability date

June 2014

Summary of evidence on comparative efficacy

Dabigatran etexilate (referred to as dabigatran hereafter) is a direct thrombin inhibitor, administered orally without the need for routine anticoagulant monitoring, after ≥5 days of parenteral anticoagulation.[1] Rivaroxaban, a direct inhibitor of activated factor X, is also licensed for the treatment of DVT and PE, and prophylaxis of recurrent DVT and PE, and has been accepted for use by SMC for this indication.[2] Other medicines for treatment or prophylaxis of recurrent DVT and PE include low molecular weight heparin (LMWH) followed by warfarin.

Two similarly designed, phase III, double-blind comparative studies (RE-COVER and RE-COVER II) have been conducted in patients with acute objectively verified DVT of the leg involving proximal veins, and/or PE, for whom at least six months of anticoagulant therapy was considered appropriate.[3-5] All patients received initial treatment with a parenteral anticoagulant (unfractionated heparin intravenously [iv] or low molecular weight heparin subcutaneously [sc] for 5 to 10 days). Patients were randomised equally (stratified by presence or absence of symptomatic PE; and of active cancer) to oral treatment with dabigatran 150mg twice daily or warfarin, dose adjusted to achieve an INR of 2.0 to 3.0 for six months. Overall, in both studies, around 70% had a DVT only, 20% had a PE only and 10% had PE + DVT.

The primary endpoint was the proportion of patients with recurrent symptomatic venous thromoembolism events (VTE) and death related to VTE from randomisation to day 180. The studies were designed to test non-inferiority of the primary endpoint comparing the upper boundary of the 95% confidence interval (CI) for the hazard ratio (HR) with the predefined margin of 2.75, and the upper boundary of the 95% CI for the difference in risk with the predefined margin of 3.6%. Dabigatran was shown to be non-inferior to warfarin in both studies. Results of the primary and key secondary endpoints are included in table 1 for the individual studies and pooled analysis.

Table 1: primary and key secondary endpoints for RE-COVER, RE-COVER II and pooled analysis

	RE-COVER		RE-COVER II		Pooled analysis	
	dabigatran	**warfarin**	**dabigatran**	**warfarin**	**dabigatran**	**warfarin**
Primary endpoint (to day 180)						
Symptomatic VTE and death related to VTE; % (n/N)	2.4% (30/1274)	2.1% (27/1265)	2.3% (30/1279)	2.2% (28/1289)	2.4% (60/2553)	2.2% (55/2554)
Hazard ratio, 95% CI	1.10 95% CI 0.65 to 1.84		1.08 95% CI 0.64 to 1.8		1.09 95% CI 0.76 to 1.57	
Risk difference, 95% CI	0.4% 95% CI -0.8 to 1.5		0.2% 95% CI -1.0 to 1.3		NR	
Secondary endpoints						
Symptomatic recurrent DVT; % (n/N)	1.3% (16/1274)	1.4% (18/1265)	2.0% (25/1279)	1.3% (17/1289)	1.6% (40/2553)†	1.3% (34/2554)†
	HR 0.87, 95% CI 0.44 to 1.71		HR1.48 95% CI 0.80 to 2.74		NR	
Symptomatic non-fatal PE; % (n/N)	1.0% (13/1274)	0.6% (7/1265)	0.6% (7/1279)	1.0% (13/1289)	0.7% (18/2553)†	0.7% (18/2554)†
	HR 1.85, 95% CI 0.74 to 4.64		HR 0.54 95% CI 0.21 to 1.35		NR	
Deaths related to PE; % (n/N)	0.1% (1/1274)	0.2% (3/1265)	0.08% (1/1279)*	nil	0.1% (2/2553)	0.1% (3/2554)
	HR 0.33, 95% CI 0.03 to 3.15		NR		NR	
All deaths; % (n/N)	1.6% (21/1274)	1.7% (21/1265)	2.0% (25/1279)	1.9% (25/1289)	1.8% (46/2553)	1.8% (46/2554)
	HR 0.98, 95% CI 0.53 to 1.79		HR 0.98 95% CI 0.56 to1.71		HR 1.0, 95% CI 0.67 to 1.51	

VTE=venous thromboembolism, DVT=deep vein thrombosis, PE=pulmonary embolism, CI=confidence interval, HR=hazard ratio, NR=not reported

*there were two additional deaths in single-dummy phase, before dabigatran was started.

† events contributing to the primary end point; in the case of a patient suffering 2 different events, the first event is counted.

A further two phase III randomised, double-blind, studies have been conducted to assess the long-term treatment and secondary prevention of symptomatic VTE.[3,6,7] Both studies recruited patients who had had an acute symptomatic DVT or PE 3 to 12 months prior to screening, and had been treated with an approved anticoagulant or dabigatran (for patients enrolled in RE-COVER or RE-COVER II) for between 3 and 12 months in RE-MEDY, and 6 to 18 months in RE-SONATE. RE-MEDY recruited patients at increased risk of recurrent VTE on the basis of the site investigator's assessment, and they were randomised equally (stratified by presence or absence of cancer and diagnosis of DVT or PE) to dabigatran or warfarin (doses as for previous studies) for 6 to 36 months. RE-SONATE excluded patients with cancer and randomised patients equally (stratified by study centre) to treatment with dabigatran 150mg orally twice daily or placebo for up to 12 months. In RE-MEDY, around 65% had a

DVT only, 23% had a PE only and 12% had PE and DVT, and in RE-SONATE, the respective proportions were 63%, 27% and 5.3%.

The primary endpoint was recurrent and objectively verified VTE or death associated with VTE (RE-MEDY) or unexplained death (RE-SONATE). A pre-defined non-inferiority margin of 2.85 for the hazard ratio and 2.8% for risk difference (at 18 months) was used for RE-MEDY. The mean exposure to study drug was around 474 days (RE-MEDY) and 164 days (RE-SONATE). Dabigatran was demonstrated to be non-inferior to warfarin and was superior to placebo in RE-MEDY and RE-SONATE respectively. Primary and key secondary endpoints are included in table 2.

Table 2: Primary and key secondary endpoints for RE-MEDY and RE-SONATE studies

	RE-MEDY		**RE-SONATE**	
	dabigatran	**warfarin**	**dabigatran**	**placebo**
Primary endpoint,% (n/N)	1.8% (26/1430)	1.3% (18/1426)	0.4% (3/681)	5.6% (37/662)
Hazard ratio, 95% CI	1.44, 95% CI 0.78 to 2.64		0.08, 95% CI 0.02 to 0.25	
Risk difference 95% CI	0.38%, 95% CI -0.50 to 1.25		NR	
Secondary endpoints				
Symptomatic recurrent DVT; % (n/N)	1.2% (17/1430)	0.9% (13/1426)	0.3% (2/681)	3.3% (22/662)
	HR 1.32, 95% CI 0.64 to 2.71		NR	
Symptomatic non-fatal PE; % (n/N)	0.7% (10/1430)	0.4% (5/1426)	0.1% (1/681)	2.1% (14/662)
	HR 2.04, 95% CI 0.70 to 5.98		NR	
Deaths related to VTE; % (n/N)	0.1% (1/1430)	0.1% (1/1426)	NR	NR
	HR 1.01, 95% CI 0.06 to 16.2		NR	
Death due to any cause; % (n/N)	1.2% (17/1430)	1.3% (19/1426)	NR	NR
	HR 0.90, 95% CI 0.47 to 1.72		NR	

Primary endpoint was recurrent and objectively verified VTE or death associated with VTE (RE-MEDY); recurrent and objectively verified VTE or unexplained death (RE-SONATE). VTE=venous thromboembolism, DVT=deep vein thrombosis, PE=pulmonary embolism, CI=confidence interval, HR=hazard ratio, NR=not reported

Summary of evidence on comparative safety

In pooled analysis of RE-COVER and RE-COVER II (from start of any study drug, i.e. single- and double-dummy periods) a major bleeding event occurred in 1.4% (37/2553) of dabigatran treated patients and 2.0% (51/2554) of warfarin treated patients; HR 0.73, 95% CI 0.48 to 1.11). [5] Intracranial bleeding occurred in 0.1% (2/2553) versus 0.2% (5/2554) of patients respectively. A major or clinically relevant non-major bleeding event occurred in 5.3% (136/2553) versus 8.5% (217/2554) of patients

respectively; HR 0.62, 95% CI 0.50 to 0.76. Any bleeding event occurred in 16% (411/2553) versus 22% (567/2554) of patients respectively; HR 0.70, 95% CI 0.61 to 0.79. Any acute coronary syndrome occurred in 0.4% (9/2553) versus 0.2% (5/2554) of patients treated with dabigatran and warfarin respectively and myocardial infarction in 0.3% (8/2553) versus 0.2% (4/2554) of patients respectively.

In RE-COVER, there was no significant difference between groups in frequency of any AE, with the exception of dyspepsia in (3.1% versus 0.7%) which also occurred in higher proportion of dabigatran patients in RE-COVER II (1.0% versus 0.2%). [4,5]

In RE-MEDY, major bleeding events occurred in 0.9% (13/1430) of dabigatran treated patients and 1.8% (25/1426) of warfarin treated patients; HR 0.52, 95% CI 0.27 to 1.02).[6] A major or clinically relevant bleeding event occurred in 5.6% (80/1430) versus 10% (145/1426) of patients respectively; HR 0.54, 95% CI 0.41 to 0.71. Any bleeding event occurred in 19% (277/1430) versus 26% (373/1426) of patients respectively; HR 0.71, 95% CI 0.61 to 0.83. There was a significantly higher rate of acute coronary syndrome events in the dabigatran group (0.9% [13/1430], 10 myocardial infarction, three unstable angina) than in the warfarin group (0.2% [3/1426], one myocardial infarction, two unstable angina). The majority were considered related to study treatment, with the exception of myocardial infarction in one patient in the dabigatran group and unstable angina in one patient in the warfarin group.

Summary of clinical effectiveness issues

Dabigatran, as well as rivaroxaban, is licensed for the treatment of DVT and PE and the prophylaxis of recurrent DVT/PE and does not require routine anticoagulant monitoring. Dabigatran has previously been accepted by SMC for the primary prevention of VTE after elective total hip or knee replacement surgery and the prevention of stroke and systemic embolism in non-valvular atrial fibrillation.

In two phase III studies which compared dabigatran to warfarin for treatment of DVT/PE, non-inferiority was demonstrated for the primary endpoint of recurrent symptomatic VTE and deaths related to VTE. There were significantly fewer major or clinically relevant non-major bleeding events for dabigatran-compared to warfarin-treated patients. The primary outcome is recommended in European Medicines Agency guidance for the clinical investigation of medicinal products for the treatment of acute venous thromboembolism.[8] In the active comparator study for prophylaxis of recurrent DVT/PE, non-inferiority was demonstrated and there were significantly fewer major or clinically relevant non-major bleeding events for dabigatran- compared to warfarin-treated patients. The majority of patients across all studies had DVT only (63% to 69%); the proportion of patients with a PE was 21% to 27% and DVT and PE was 5.3% to 12%.

In the RE-COVER study, the median length of treatment with parenteral anticoagulant before dabigatran was initiated was 9 days, and in RE-COVER II the mean length of treatment was around 9.5 days. This is longer than the treatment duration of parenteral anticoagulant generally used with warfarin (when heparin and warfarin are started together). However, the duration of heparin therapy (5 days as compared with 10 days) has not been shown to influence the efficacy of long-term anticoagulation. [4] In pooled analysis of RE-COVER and RE-COVER II, the efficacy of dabigatran compared to warfarin was lower in patients aged <60 years and higher in patients aged >60 years, although there were no statistically significant differences at any age.

In the RE-MEDY study, the pre-specified non-inferiority margin was large (2.85), allowing an increase in risk by a factor of nearly 3 to be accepted as non-inferior. The study authors noted that this was a limitation of the study design. They also noted that large non-inferiority margins had been used in

short-term studies; e.g. in the RE-COVER/RE-COVER II studies the non-inferiority margin was 2.75 and in the rivaroxaban studies the non-inferiority margin was 2.0. [9,10].

There are no direct comparative data for dabigatran versus rivaroxaban. The submitting company undertook adjusted indirect comparisons (AIC) that compared dabigatran with rivaroxaban for the treatment of DVT and PE and secondary prevention of recurrent VTE. The endpoints included recurrence of VTE, major bleeding, and major bleeding episode/clinical relevant bleeding episode. Due to issues relating to heterogeneity, the AIC results were not used in the economic model presented in the company's submission; however, their inclusion was requested by the assessment team.

The AIC of dabigatran versus rivaroxaban for the treatment of DVT and PE has been published[11] and included four studies: RE-COVER/ RE-COVER II and two rivaroxaban studies (EINSTEIN-PE[9] and EINSTEIN-DVT[10]). For dabigatran versus rivaroxaban the relative risk (RR) of VTE or VTE-related deaths was 1.23 (95% CI 0.69 to 2.19). Other endpoints included major bleeding episode, RR1.37 (95% CI 0.77 to 2.45), and major bleeding episode/clinical relevant bleeding episode RR0.68 (95% CI 0.53 to 0.86). However, heterogeneity for treatment effects in the rivaroxaban studies was considered to be high for the following: VTE or VTE-related deaths I^2=61.9%, p=0.11; all cause mortality I^2=50%, p=0.16. The AIC for secondary prevention of recurrence of VTE in low risk patients included the RE-SONATE and the EINSTEIN-Ext studies.[10]

The summary of product characteristics for dabigatran notes that efficacy and safety have not been established for DVT/PE patients with active cancer. In the active comparator studies, approximately 4% of patients had active cancer. Furthermore there are no efficacy or safety data for the use of 110mg twice daily dose for the indication under review.[1]

Dabigatran is given at a dose of 150mg twice daily (or 110mg twice daily in certain patient groups) following treatment with a parenteral anticoagulant for ≥5 days. This compares with rivaroxaban which is given at a dose of 15mg twice daily for three weeks, then 20mg once daily and has the advantage of no requirement for initial parenteral anticoagulation.[1,2]

Summary of comparative health economic evidence

The company submitted a cost-utility analysis comparing dabigatran with warfarin, both preceded by parenteral anticoagulant treatment with LMWH, and with rivaroxaban. Separate economic analyses were performed for the treatment of acute VTE, and for long term treatment for the secondary prevention of recurrent VTE (rVTE). A lifetime horizon was used (60 years).

The HRs for rVTE (DVT and PEs), intracranial haemorrhage, and major or clinically relevant bleeding events were derived using data from the comparative trials versus warfarin. For the comparison with rivaroxaban, the HRs were based on applying treatment effect data from individual dabigatran and rivaroxaban trials to baseline risk from the control arms of the dabigatran trials. The risks of rVTE and bleeding events were adjusted based on an assumption that patients on warfarin would spend 58% of time on treatment in the INR range of 2.0-3.0. Data on probabilities of other clinical events including severe post-thrombotic syndrome and chronic thromboembolic pulmonary hypertension were derived from published sources. VTE and bleeding related mortality was estimated. Disutility estimates were included for primary and recurrent VTE (-0.25), ICH with disability (-0.5), major bleeds (-0.13) and clinically relevant non-major bleeds (-0.04) based on analysis of EQ- 5D data in the dabigatran trials. Other health state disutilities were derived from published studies, with a disutility assumed for being on warfarin treatment (of -0.012) based on a published time-trade off study.

Resource use included drug acquisition costs, costs of parenteral anticoagulation treatment administration based on 5 days treatment (either within hospital or home administered), INR monitoring, hospital inpatient stay for primary and rVTEs and other clinical events, and resource use for the management of bleeding events. Visits to the anticoagulation clinic for INR monitoring for warfarin were assumed to be 5 visits covering the titration phase of warfarin treatment, and 1 visit per month for the remainder of the treatment period. This was based on expert clinical opinion. Maximum treatment duration was based on clinical trial durations – 6 months for dabigatran and warfarin, and between 3-12 months for rivaroxaban for the treatment of VTE, and between 6-18 months for each treatment for the secondary prevention of rVTE.

The results for the treatment of VTE analysis were an estimated incremental cost-effectiveness ratio (ICER) of £862 per quality-adjusted life-year (QALY) gained versus warfarin, with an incremental cost of £21 and incremental QALYs of 0.0239, and dabigatran was estimated to be dominant (i.e. more effective and less costly) versus rivaroxaban with estimated savings of £20 and incremental QALYs of 0.0003 per patient. The results for the secondary prevention of rVTE analysis were an ICER of £8,319/QALY gained vs. warfarin, with an incremental cost of £458 and incremental QALYs of 0.0551 per patient (i.e. equivalent 20 days benefit), and dabigatran was estimated to be dominant versus rivaroxaban with estimated savings of £67 and incremental QALYs of 0.0020. In both the analyses versus warfarin, dabigatran was associated with higher drug costs largely offset by lower monitoring costs (for INR control), and lower relative costs and QALY gains associated with fewer overall bleeding events estimated. In the analyses versus rivaroxaban, dabigatran was associated with slightly lower drug costs than rivaroxaban, but higher acute parenteral anticoagulation costs. The small cost savings and QALY gains estimated were largely due to fewer estimated overall bleeding events with dabigatran.

Scenario analysis demonstrated that results were potentially sensitive to the time horizon adopted, with a ten year horizon resulting in a cost/QALY of £3.2k/QALY versus warfarin, and £19.7k/QALY versus rivaroxaban for the treatment of acute VTE (albeit based on extremely small differences in costs and QALYs), and £13.8/QALY vs warfarin for the long term treatment and the secondary prevention of rVTE, although dabigatran still dominated rivaroxaban in this analysis. The secondary prevention results were also sensitive to a scenario of no utility decrement assumed for warfarin treatment, which increased the ICER to £15k/QALY versus warfarin. In most scenarios explored, dabigatran remained dominant compared to rivaroxaban, although reducing ICH disutility or duration of other bleeds disutility resulted in dabigatran having lower costs but lower effectiveness than rivaroxaban in acute VTE treatment and secondary prevention of rVTE. Probabilistic Sensitivity Analysis indicated a probability of dabigatran being considered cost-effective at a threshold of £20k/QALY of 93% versus warfarin and 54% versus rivaroxaban in the treatment of VTE, and 93% and 80% respectively for the secondary prevention of rVTE.

The main issues with the economic analysis were:

- An AIC was performed for the comparisons with rivaroxaban. However, the HR estimates from this were not used in the economic model and, in essence, a naïve indirect comparison approach was used instead. As this is not considered robust, on request, the company provided an analysis using the AIC generated HRs for VTE and bleeding event rates, including an analysis in which only statistically significant HRs were included. The finding from this analysis confirmed the findings from the naïve indirect comparison of extremely small differences in costs and QALYs between dabigatran and rivaroxaban.
- The analysis performed versus warfarin includes non-significant HRs – hence the company was requested to perform analyses including only statistically significant HRs (this is for major clinically relevant bleeds for the treatment of VTE analysis). This resulted in improved ICERs versus warfarin of £463/QALY and £7,375/QALY for the acute treatment and secondary prevention analyses respectively due to the exclusion of non-significant hazard ratios for rVTE that were greater than one for dabigatran versus rivaroxaban.

- In the base case comparisons against rivaroxaban, the company assumed the same length of hospital stay for the primary DVT or PE. However, length of stay (LOS) might be expected to be relatively shorter with rivaroxaban due to there being no requirement to administer acute parenteral anticoagulation. The company provided supplementary analysis to show the impact of assuming shorter lengths of stay for rivaroxaban treatment. Threshold analysis indicated that the reduction in length of stay with rivaroxaban would have to be greater than 25% for either acute or secondary prevention treatment with dabigatran to exceed £30k per QALY. This analysis also removes any non-significant differences.

SMC noted that LOS was not a major issue given that, in Scotland, unless hospital admission is indicated by the clinical condition of the patient, anticoagulation, oral or parenteral, is often given on an outpatient basis. The economic case has therefore been demonstrated.

Summary of patient and public involvement

The following information reflects the views of the specific patient group.

- Submissions were received from Anticoagulation Europe (ACE) and Lifeblood: The Thrombosis Charity, which are both registered charities.

- ACE and Lifeblood: The Thrombosis Charity have both received funding from several pharmaceutical companies in the past two years, including from the submitting company.

- The effects of venous thrombosis including pain, swelling, and tenderness, inability to walk, cramp, and skin irritation are factors that disrupt people's lives leading to hospitalisation and the need for substantial carer support. Untreated PE can be fatal and those who survive a PE may require intensive care and recovery can take up to several months.

- People's experience is that current treatment regimes are complex to manage, requiring regular monitoring by blood tests to control risk of bleeding or clotting. They may also require intense dosing adjustments and may experience problems relating to receiving anticoagulant drugs by injection. Dietary and drug regimes may also need to be considered to help the patient achieve the required levels.

- Potential advantages of the new medicine include: standard daily dosing which does not require adjustment; reduced risk of bleeding; no requirement for hospital visits and monitoring; reduced contra-indications. These issues are of wide benefit, but particularly to those requiring indefinite anticoagulation therapy.

Additional information: guidelines and protocols

The Scottish Intercollegiate Guidelines Network (SIGN) published guideline 122; Prevention and management of venous thromboembolism in December 2010. [12]

- Patients with suspected PE should be treated with therapeutic doses of heparin or fondaparinux until the diagnosis has been deemed very unlikely.
- Once confirmed the heparin or fondaparinux should be continued until the INR is at least 2.0 on a vitamin K antagonist, and for at least 5 days.
- Patients with suspected DVT should be treated with therapeutic doses of LMWH or fondaparinux until the diagnosis has been deemed very unlikely or confirmed.

- In confirmed DVT the heparin or fondaparinux should be continued until the INR is at least 2.0 on a vitamin K antagonist, and for at least 5 days.
- Intravenous unfractionated heparin may be an appropriate alternative in certain circumstances, e.g. if thrombolysis is being considered, in the immediate postoperative period or where there is particular risk of bleeding.
- Patients with cancer and VTE should be offered treatment with LMWH (rather than vitamin K antagonist) for three to six months and reviewed thereafter.
- After a first episode of proximal limb deep vein thrombosis or pulmonary embolism, treatment with a vitamin K antagonist should be continued for at least three months.

The British Committee for Standards in Haematology published the fourth edition of guidelines on oral anticoagulation with warfarin in 2011.[13] Treatment of VTE with warfarin should initially also include at least five days of parenteral anticoagulation (LMWH, unfractionated heparin or fondaparinux), continuing until the INR is ≥2.0. The first episode of VTE should be treated with an INR target of 2.5 and for a minimum duration of three months. Patients with unprovoked PE should be considered for long term anticoagulation, the individual patient's risk of recurrence and bleeding should be taken into account.

Additional information: comparators

Rivaroxaban, or LMWH plus warfarin.

Cost of relevant comparators

Drug	Dose Regimen	Cost (£) for 7 to 10 days treatment	Cost (£) for 6 months treatment
Dabigatran	**150mg orally twice daily**		**400***
Rivaroxaban	15mg orally twice daily for 21 days then 20mg orally once daily		426
Warfarin	orally as determined by prothrombin time**		3
Dalteparin	15,000 units once daily sc injection	59 to 85	
Enoxaparin	1.5mg/kg once daily sc injection	68 to 98	
Tinzaparin	175 units/kg once daily sc injection	83 to 119	

Doses are for general comparison and do not imply therapeutic equivalence. Costs from eVadis on 20 June 2014. Costs are based on doses calculated for a 70kg adult. sc=subcutaneous

*Cost excludes cost of parenteral anticoagulation; **Average daily dose of warfarin is around 5mg (range 1 to 15mg)[14]

Additional information: budget impact

The submitting company estimated there to be 26,022 patients eligible for treatment with dabigatran in each year to which an estimated uptake rate was applied.

The submitting company estimated the gross medicines budget impact to be £44k in year 1 and £560k in year 5. As other medicines were assumed to be displaced, the net medicines budget impact was estimated to be £43k in year 1 and £553k in year 5.

*Other data were also assessed but remain commercially confidential.**

References

The undernoted references were supplied with the submission.

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14. Scottish Intercollegiate Guidelines Network. SIGN Guideline 129 Antithrombotics: indications and management. August 2012

This assessment is based on data submitted by the applicant company up to and including 15 August 2014.

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.