Cost-effectiveness of Apixaban Compared With Edoxaban for Stroke Prevention in Nonvalvular Atrial Fibrillation

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ABSTRACT

Purpose: The purpose of this analysis was to assess the cost-effectiveness of apixaban 5 mg BID versus high- and low-dose edoxaban (60 mg and 30 mg once daily) as intended starting dose strategies for stroke prevention in patients from a UK National Health Service perspective.

Methods: A previously developed and validated Markov model was adapted to evaluate the lifetime clinical and economic impact of apixaban 5 mg BID versus edoxaban (high and low dose) in patients with nonvalvular atrial fibrillation. A pairwise indirect treatment comparison was conducted for clinical end points, and price parity was assumed between apixaban and edoxaban. Costs in 2012 British pounds, life-years, and quality-adjusted life-years (QALYs) gained, discounted at 3.5% per annum, were estimated.

Findings: Apixaban was predicted to increase life expectancy and QALYs versus low- and high-dose edoxaban. These gains were achieved at cost-savings versus low-dose edoxaban, thus being dominant and nominal increases in costs versus high-dose edoxaban. The incremental cost-effectiveness ratio of apixaban versus high-dose edoxaban was £6763 per QALY gained.

Implications: Apixaban was deemed to be dominant (less costly and more effective) versus low-dose edoxaban and a cost-effective alternative to high-dose edoxaban. (*Clin Ther*. 2015;37:2476–2488) © 2015 The Authors. Published by Elsevier HS Journals, Inc.

Key words: apixaban, atrial fibrillation, clinical impact, cost-effectiveness, edoxaban.

INTRODUCTION

Nonvalvular atrial fibrillation (NVAF) is the most common sustained cardiac arrhythmia and a major cause of stroke and thromboembolism, associated with increased mortality, increased morbidity, and high medical costs.[1,2] Anticoagulation treatment is therefore recommended to mitigate the risk of stroke.[3]

The 2012 European Society of Cardiology guidelines recommend the consideration of the non–vitamin K oral anticoagulants (NOACs) dabigatran, rivaroxaban, and apixaban, for the prevention of stroke in patients[3] with NVAF because they offer relative efficacy, tolerability, and convenience by addressing certain limitations associated with traditional vitamin K antagonists (VKAs).

The NOACs have been compared with VKAs in large Phase III randomized trials. The Randomized Evaluation of Long-term Anticoagulation Therapy[4] trial revealed superiority for dabigatran 150 mg BID and noninferiority for dabigatran 110 mg BID versus dose-adjusted VKAs in reducing the primary efficacy end point of stroke and systemic embolism. In addition, dabigatran 110 mg was superior to dose-adjusted VKAs in reducing the risk of major hemorrhage, whereas dabigatran 150 mg[4] was noninferior. The Rivaroxaban Once Daily Oral Direct Factor Xa

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Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation[5] trial found rixaroxaban 20 mg once daily to be noninferior to dose-adjusted VKAs in efficacy and tolerability. The Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE)[6] trial found that apixaban 5 mg BID was superior to dose-adjusted VKAs in reducing stroke and systemic embolism, major bleeding, and all-cause death. Finally, the Phase III Study of Apixaban in Patients With Atrial Fibrillation (AVERROES)[7] trial, evaluating apixaban 5 mg BID versus aspirin, in VKA-unsuitable patients, found apixaban's superiority to aspirin in reducing the risk of stroke and systemic embolism without significantly increasing the risk of major hemorrhage.[7] Lack of monitoring requirement and strength of efficacy-tolerability data as observed in NOAC trials resulted in the European Society of Cardiology guidelines recommendation of NOACs instead of dose-adjusted VKA treatment.[3]

None of the NOACs has been evaluated against each other in head-to-head trials. Indirect treatment comparisons (ITCs) have indicated no significant differences between the NOACs in efficacy[8,9]; however, they found a reduced risk of major bleeding among patients treated with apixaban or dabigatran 110 mg compared with dabigatran 150 mg and rivaroxaban.[8–10] Apixaban is the only NOAC that received a Class 1, Evidence A classification from the American Heart Association/American Stroke Association because it appears to have the best combination of efficacy and tolerability at the tested doses.[11] However, no clear recommendation for the use of one NOAC over another is provided; rather, cost is highlighted as an important consideration in the choice of agent.[3]

Most evaluations comparing a NOAC against dose-adjusted VKAs for stroke prevention in patients with NVAF concluded that the NOACs offer superior benefits and were cost-effective compared with dose-adjusted VKAs.[12–15] In addition, studies that compared cost-effectiveness among the NOACs suggest that apixaban may be the most cost-effective NOAC (compared with rivaroxaban and dabigatran 150 mg and 110 mg) for stroke prevention among patients with NVAF.[13–15]

A recently introduced NOAC, edoxaban, is another oral factor Xa inhibitor that has been studied in dosages of 30 mg once daily (low dose) and 60 mg once daily (high dose) versus dose-adjusted VKAs in a double-blind randomized clinical trial called Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation (ENGAGE-AF)—Thrombolysis in Myocardial Infarction 48 (TIMI-48)[16] and has recently received European marketing authorization.[17] Low-dose edoxaban was numerically worse whereas high-dose edoxaban once daily was numerically better than dose-adjusted VKAs in reducing stroke and systemic embolism. Both doses resulted in significantly less bleeding.[16] Comparatively, low-dose edoxaban had a better bleeding profile but worse stroke prevention than high-dose edoxaban.[16]

A recently published ITC[10] reported that a high-dose edoxaban regimen was broadly comparable in efficacy to apixaban and dabigatran 110 mg, but apixaban was associated with lower risks of major or clinically relevant nonmajor gastrointestinal bleeding. High-dose edoxaban was broadly comparable in efficacy and tolerability to dabigatran 110 mg BID but had lower efficacy compared with dabigatran 150 mg. There were no differences in efficacy end points between high-dose edoxaban and rivaroxaban, but the latter was associated with more bleeding. Low-dose edoxaban was less efficacious compared with apixaban, dabigatran 150 mg, and rivaroxaban but had fewer major bleedings and was generally more tolerable than all the other alternatives.

The addition of edoxaban to the options of available NOACs may change the relative value of these NOACs from a payer perspective. A holistic assessment of clinical benefits versus risks extrapolated over lifetime is required to determine the relative value and overall clinical benefit of various NOACs. The aim of this study was to reexamine the hypothesis that apixaban may be the most cost-effective NOAC, taking the emergence of edoxaban into account. We therefore assessed the cost-effectiveness of apixaban 5 mg BID versus edoxaban (low dose and high dose) as intended starting-dose strategies for stroke prevention in patients with NVAF from the UK National Health Service (NHS) payer perspective.

METHODS

A previously developed and validated[18,19] Markov model[12,13] was adapted to evaluate the lifetime clinical and economic impact of apixaban versus edoxaban (low and high dose) in patients with NVAF.