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▼ Pradaxa® (dabigatran etexilate), the first new oral anticoagulant in over 50 years, has been accepted for use by the Scottish Medicines Consortiumⁱ

AF is the most common heart rhythm condition in the UK,ⁱⁱ affecting 75,000 people in Scotland,ⁱⁱⁱ and is a leading cause of strokeⁱⁱ

Bracknell, UK [Monday, 12th September] Pradaxa®, the first new oral anticoagulant in over 50 years licensed for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (AF) and one or more risk factors (please see notes to editors), has been accepted by the Scottish Medicines Consortium (SMC) for use within NHS Scotland (<http://www.scottishmedicines.org.uk/Home>).ⁱ

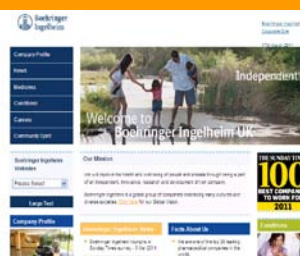
The decision made by the SMC for Pradaxa marks an important step in managing care of patients with AF, which is the most common heart rhythm condition in the UK and a leading cause of stroke.ⁱⁱ

Professor Adrian Brady consultant cardiologist, Department of Medical Cardiology, Glasgow Royal Infirmary comments, " This is excellent news for eligible patients in Scotland who will now have access to Pradaxa, a new anticoagulant. AF affects 2% of the population and about 50% of the patients who suffer from a stroke die from that stroke within the first few days or weeks while 50% of those who survive have some level of disability at six months. This decision marks a significant advance for patients and clinicians affected by AF."

Stroke (of which an estimated 15% are caused by AF^{iv}) is one of the top three causes of death and the largest cause of adult disability costing



Contact:
Boehringer Ingelheim Limited
Communications
Ellesfield Avenue
Bracknell
Berks
RG12 8YS
Phone: +44 (0)1344 742779



More information
www.boehringer-ingelheim.co.uk

the NHS over £3 billion a year. ^v It is estimated that 1,950 strokes per year in Scotland^{vi} and 22,500 strokes per year in the UK are directly attributable to AF.^{vii} 75,000 patients in Scotland are diagnosed with AF. An estimated 40,000 (53%) are prescribed an oral anticoagulant^{viii} and 29,000 (38%) who should be prescribed an oral anticoagulant are not receiving it. The estimated average cost of a stroke for a patient with AF is £11,000 (health-care costs up to three months post event). For a disabling stroke, the average annual follow-up costs are in excess of £14,000 per patient per year. ^{ix}

Trudie Lobban MBE, founder and CEO of the Atrial Fibrillation Association comments: "Our members live in fear of suffering a disabling or fatal stroke and they have waited years for an alternative treatment option."

The EU licence for Pradaxa was granted on 1st August 2011 for the prevention of stroke and systemic embolism in eligible adult patients with AF (please refer to notes to editors for description of the licensed indication).^{xiii} The granting of the licence follows the submission of data from the RE-LY trial - a phase III stroke prevention in AF trial published to date involving 18,113 patients enrolled in 951 centres in 44 countries. ^{x,xi}

The primary endpoint of the RE-LY trial was incidence of stroke and systemic embolism. The study showed the recommended dose of Pradaxa 150mg, twice daily reduced the relative risk of stroke or systemic embolism by 35% in eligible AF patients compared to warfarin (1.71% per year with warfarin to 1.11% per year with Pradaxa 150mg, a 0.6% per year absolute reduction in risk {ARR} which is a 35% per year relative risk reduction {RR}; $p < 0.001$). The primary safety outcome measure in RE-LY, major haemorrhage, was comparable in the Pradaxa 150mg twice daily group and the warfarin group. ^{x,xi}

In the RE-LY study, Pradaxa 110mg, twice daily, (a dose for specific patients - please see notes to editors), demonstrated similar reductions in stroke and systemic embolism compared to warfarin, while delivering a 20% per year reduction ($p=0.003$) in major bleeding rates compared to warfarin: the rate of major bleeding was 3.36% per year in the warfarin group, as compared with 2.71% per year in the group receiving 110 mg of dabigatran ($p= 0.003$), an ARR of 0.65%.^{x,xi}

Pradaxa will provide clinicians with a new treatment option for stroke prevention in AF that does not require frequent coagulation monitoring, dose changes or routine adjustment, and dietary restrictions.^{xii}

-Ends-

For further information please refer to notes to editors

For further information, please contact:

Bridget Mullahy	Alison MacKenzie
Communications Manager	Managing Director
Boehringer Ingelheim Limited	Reynolds-MacKenzie
Tel: +44 (0)1344 74 1155	Tel: + 44 (0) 20 3427 5795

Notes to Editors:

About Pradaxa®^{xiii}

Pradaxa 150mg twice daily is licensed in the UK for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation with one or more of the following risk factors:ⁱ

- previous stroke, transient ischemic attack, or systemic embolism (SEE)
- left ventricular ejection fraction < 40 %
- symptomatic heart failure \geq New York Heart Association (NYHA) Class 2
- age \geq 75 years
- age \geq 65 years associated with one of the following: diabetes mellitus, coronary artery disease, or hypertension

Pradaxa 110 mg twice daily - for patients over 80 years or those taking concomitant verapamil and could be considered for other patient groups including those:^{xiv}

- who are 75-80 years with an increased risk of bleeding
- with gastritis, esophagitis or gastroesophageal reflux, active ulcerative gastrointestinal (GI) disease or recent GI bleeding
- with moderate renal impairment (CrCl 30-50ml/min), plus an increased risk of bleeding

Please refer to the Summary of Product Characteristics (SPC) enclosed for further details on risk factors and full list of dosing scenarios.

Pradaxa costs £2.52 per day.

For more information, including an educational pack, go to www.pradaxa.co.uk or call the Pradaxa information line on 0845 6017880.

Pradaxa (110mg and 75mg) is also licensed in the UK for the primary prevention of venous thromboembolic events in adults who have undergone elective total hip or elective total knee replacement surgery.^{xiv, xv}

About RE-LY[®],^{xi}

RE-LY[®] (Randomised Evaluation of Long term anticoagulant therapY) was a global, phase III, randomised trial of 18,113 patients enrolled in over 951 centres in 44 countries, investigating whether dabigatran etexilate (150mg twice daily or 110mg twice daily) is as effective as warfarin with target INR of 2.0-3.0 for stroke prevention. Patients were followed-up in the study for a median of 2 years with a minimum of 1 year follow-up.

Following treatment with Pradaxa 150 mg twice daily (the recommended dose) there was a statistically significant reduction in the incidence of stroke/systemic embolism (primary efficacy endpoint), compared with warfarin (1.11% per year vs 1.71% per year respectively; $p < 0.001$, absolute risk reduction (ARR) = 0.6% per year). The rates of major bleeding events (primary safety endpoint) were comparable between Pradaxa 150mg twice daily and warfarin (3.32% per year vs 3.57% per year; $p = 0.31$, ARR= 0.25% per year).

Following treatment with Pradaxa 150 mg twice daily there was also a statistically significant reduction in haemorrhagic stroke (0.10% per year vs 0.38% per year respectively; $p < 0.001$, ARR = 0.28% per year) and a statistically significant reduction in vascular mortality, compared with warfarin (2.43% per year vs 2.69% per year respectively; $p = 0.04$, ARR = 0.26% per year). In addition there were significantly fewer total bleeds (16.56% per year vs 18.37% per year; $p = 0.002$, ARR = 1.81% per year), life threatening bleeds (1.49% per year vs 1.85% per year; $p = 0.03$, ARR = 0.36% per year) and intracranial bleeds (0.32% per year vs 0.76% per year; $p < 0.001$, ARR = 0.44% per year) than in patients treated with

warfarin. However, the incidence of gastrointestinal bleeding was higher in these patients than in those treated with warfarin (1.56% per year vs 1.07% per year; $p = 0.001$, an increase in absolute risk of 0.49% per year). Although the incidence of myocardial infarction was slightly higher in the patients treated with Pradaxa 150mg than in those treated with warfarin, (97 in 6076 vs 75 in 6022 respectively; equivalent to 0.81% per year vs 0.64% per year, absolute increase in risk = 0.17% per year) this difference was not statistically significant ($p = 0.12$).

In patients treated with Pradaxa at 110mg twice daily, the rates of stroke or systemic embolism were comparable to those seen in patients treated with warfarin (1.54% per year vs 1.71% per year; $p < 0.001$, ARR = 0.29% per year). Major bleeding rates (2.87% per year vs 3.57% per year; $p = 0.003$, ARR = 0.07% per year) were significantly lower.

The only adverse event that was significantly more common with Pradaxa than with warfarin was dyspepsia. Dyspepsia occurred in 348 patients (5.8%) in the warfarin group and in 707 patients (11.8%) and 688 patients (11.3%) in the 110mg and 150mg Pradaxa groups respectively ($p < 0.001$ for both comparisons).

Please refer to the results of the RE-LY study in the New England Journal of Medicine for further information.

About AF and stroke

AF is the most common heart rhythm condition in the UK,ⁱⁱ affecting approximately 75,000 people in the Scotlandⁱⁱⁱ and is a leading cause of stroke.ⁱⁱ Approximately 150,000 people have a stroke in the UK^{xvi} each year, of which an estimated 15% are caused by AF.^{iv} Lifetime risks for development of AF are 1 in 4 for both men and women 40 years of age and older.^{xvii} The prevalence of AF rises to 10% in people over the age of 80.^{ii,xviii} People with AF are at a five-fold increased risk of suffering a stroke.^{xviii,xix} Over two million people worldwide suffer strokes related to AF each year.^{xx,iv} Strokes due to AF are more severe with an increased

likelihood of death and disability compared to non-AF stroke.^{xxi} The mortality rate of patients with AF is about double that of patients in normal sinus rhythm.^{xxix} Many AF related strokes can be prevented with appropriate antithrombotic therapy.^{xxii}

About Boehringer Ingelheim

The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 145 affiliates and more than 42,000 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel products of high therapeutic value for human and veterinary medicine.

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References:

- ⁱThe Scottish Medicines Consortium (<http://www.scottishmedicines.org.uk/Home>), Accessed September 2011
- ⁱⁱ Stewart S, Murphy N, Walker A, et al. Cost of an emerging epidemic: an economic analysis of atrial fibrillation in the UK. *Heart* 2004;90:286-92
- ⁱⁱⁱ QOF Prevalence Rates for Scotland 2009-10. ISD Scotland. Available online at <http://www.isdscotlandarchive.scot.nhs.uk/isd/6430.html> (accessed 27 May 2011)
- ^{iv} Lip GYH, Lim HS. Atrial fibrillation and stroke prevention. *Lancet Neurol* 2007;6:981-93
- ^v National Audit Office. Department of Health: Progress in improving stroke care. February 2010. Available at <http://www.nao.org.uk/publications/0910/stroke.aspx>
- ^{vi} CHSS, Stroke Information. <http://www.chss.org.uk/stroke/> (Accessed 27 May 2011)
- ^{vii} NHS Lincolnshire, <http://www.lincolnshire.nhs.uk/your-health/Strokes/> [accessed June 2011]
- ^{viii} NHS Quality Improvement Scotland. Heart Disease Improvement Programme Interim Audit of First Cycle Results 2009
- ^{ix} Dabigatran etexilate Health Improvement Model. Data on file
- ^x Connolly SJ, et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation. *N Engl J Med* 2009; 361:1139-51.
- ^{xi} Connolly SJ, Ezekowitz MD, Yusuf S, Reilly PA, Wallentin L: Newly identified events in the RE-LY® trial. *N Engl J Med* 2010; 363(19): 1875-1876 (November 4th, 2010).
- ^{xii} Stangier J. Clinical pharmacokinetics and pharmacodynamics of the oral direct thrombin inhibitor dabigatran etexilate. *Clin Pharmacokinet* 2008;47(5):285-295
- ^{xiii} Pradaxa 150 mg hard capsules SPC 2011
- ^{xiv} Pradaxa 110 mg hard capsules SPC 2011
- ^{xv} Pradaxa 75 mg hard capsules SPC 2011
- ^{xvi} The Stroke Association. Facts and figures, available at: www.stroke.org.uk/information/the_stroke_association/index.html Accessed May 2011
- ^{xvii} Lloyd-Jones DM, Wang TJ, Leip EP, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation* 2004;110:1042-6.
- ^{xviii} Fuster V, Rydn LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation - executive summary. *Circulation* 2006; 114:700-52.
- ^{xix} Kannel WB, et al. Final Draft Status of the Epidemiology of Atrial Fibrillation. *Med Clin North Am.* 2008; 92(1): 17-ix.
- ^{xx} Atlas of Heart Disease and Stroke, World Health Organization, September 2004. Accessed July 2009 at http://www.who.int/cardiovascular_diseases/en/cvd_atlas_15_burden_stroke.pdf
- ^{xxi} Lin HJ, Wolf PA, Kelly-Hayes M, et al. Stroke severity in atrial fibrillation: the Framingham study. *Stroke* 1996; 27:1760-4.
- ^{xxii} Hart RG, Benavente O, McBride R, Pearce LA. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. *Ann Intern Med* 1999; 131:492-501