

Medicines for stroke prevention in atrial fibrillation Choosing the right one for you

Atrial fibrillation (AF) is a condition that affects the heart, causing it to beat irregularly and too fast. When this happens, the heart cannot efficiently pump blood around the body. Blood can also collect in one of the heart's chambers and clot. If this happens, the clot can move and block a blood vessel somewhere else in the body (called an embolism). If this cuts off the blood supply to the brain it is known as a stroke.

Anticoagulant medicines can help to prevent the blood clotting and so prevent strokes from happening. The established standard anticoagulant is warfarin. It has been used to prevent strokes in millions of people. There are now some new anticoagulant drugs: dabigatran (Pradaxa), rivaroxaban (Xarelto), apixaban (Eliquis) and edoxaban (Lixiana).

If your doctor consider that an anticoagulant is the best treatment for your condition the information in this leaflet should help you understand about the risks and benefits of each treatment that suits you.

Not all treatment options may be suitable or possible for you depending on your particular circumstances and other medical conditions you may have, for example if you have certain types of kidney problems. Your healthcare professional will tell you if this applies to you.

The choice between warfarin, dabigatran, rivaroxaban, apixaban and edoxaban is only considered when an individual is diagnosed with 'non-valvular atrial fibrillation'.

To find out more about the treatment of Atrial Fibrillation you can contact

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References

Summary of Product Characteristics

Nice Guidelines; AF; Technology appraisals for dabigatran, apixaban, edoxaban & rivaroxaban Nice Guidelines CG 180
2014: AF Patient decision aid

Scottish Intercollegiate Guidelines Network guidelines; Prevention of stroke in patients with AF; January 2014

www.sps.nhs.uk – Compliance aids information

This leaflet lists the key information about the available treatments for preventing a stroke in patients with Atrial Fibrillation (AF). It is YOUR choice, not your doctor's decision, which medicine you take. Read through the information about the treatments and discuss it with your GP.

Generic Name	Warfarin	Dabigatran	Rivaroxaban ▼	Apixaban	Edoxaban ▼
Brand Name	Marevan	Pradaxa	Xarelto	Eliquis	Lixiana
Class of drug	All five are anticoagulants: medicines made to stop blood from clotting rapidly. They are therefore all associated with an increased risk of bleeding.				
Date of first authorisation	1950s	150mg and 110mg 2011 in UK for AF	20mg –2011 in UK for AF	2013 UK for AF	2015 in UK for AF
Black Triangle? ▼	A black triangle indicates a new medicine or one that is being used to treat new condition and so is being intensively monitored by the Medicines and Healthcare Regulatory Agency (MHRA) who oversee the safety of medicines. This is important to know about because when medicines are new, there is limited information about their safety from clinical trials. Only when large numbers of patients have taken a medicine are rare or long-term adverse effects identified. The black triangle is removed when the safety of the medicine is well established.				
	No	No	Yes	No	Yes
Strength of pills available	0.5mg, 1mg, 3mg and 5mg	110mg or 150mg	15mg or 20mg	2.5mg or 5mg	15mg or 30 mg or 60mg
How to take it	Once daily every day , dose will be tailored for you according to blood test results.	Twice daily every day , dose remains same all the time. Patients aged over 80 and patients whose kidneys work less well will take the lower dose	Once daily every day , dose remains same all the time. Patients whose kidneys work less well will take the lower dose	Twice daily every day , dose remains same all the time. Patients aged 80 and over, those less than 60kg and patients whose kidneys work less well will take the lower dose	Once daily every day , dose remains same all the time. Patients less than 60kg and patients whose kidneys work less well will take the lower dose
	If you do forget one the protective effect against strokes does not wear off as quickly as with the others	If you do forget to take your medicines, dabigatran, rivaroxaban, edoxaban and apixaban might not be the best medicines for you as the protective effect against strokes wears off quicker than warfarin			
Dosing	Dose will be tailored to the individual needs of the patient and therefore requires regular monitoring via blood tests at least 4 times a year. Some patients need as little as 1mg daily and others as much as 15mg daily. Having regular checks ensures active treatment and therefore prevention of strokes.	Available in two strengths that have predictable effects. It does not need the same amount of monitoring as warfarin but patients will have to have blood tests to assess their kidney function before and during treatment.	Available in two strengths that have predictable effects. It does not need the same amount of monitoring as warfarin but patients will have to have blood tests to assess their kidney function before and during treatment.	Available in two strengths that have predictable effects. It does not need the same amount of monitoring as warfarin but patients will have to have blood tests to assess their kidney function before and during treatment.	Available in three strengths that have predictable effects. It does not need the same amount of monitoring as warfarin but patients will have to have blood tests to assess their kidney function before and during treatment.

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How good is it at reducing strokes?	Without treatment, out of 1000 patients with AF, <i>each year</i> we expect 40-50 patients to have a stroke				
	Warfarin reduces the risk of stroke down to about 16 a year. Over a year if 1000 patients take warfarin about 24-34 patients should not have a stroke because of warfarin.	Taken regularly dabigatran 150mg BD reduces the risk of a stroke down to about 11 a year. Over a year if 1000 patients take dabigatran about 29-39 patients should not have a stroke because of dabigatran. Dabigatran 110mg BD is no better than warfarin.	Taken regularly rivaroxaban reduces the risk of stroke down to about 17 patients a year. Over a year if 1000 patients take rivaroxaban about 23-33 patients should not have a stroke because of rivaroxaban. Rivaroxaban is no better than warfarin.	Taken regularly apixaban reduces the risk of stroke down to about 13 patients a year. Over a year if 1000 patients take apixaban about 27-37 patients should not have a stroke.	Taken regularly edoxaban reduces the risk of stroke down to about 12 patients a year. In clinical trial edoxaban was as effective as warfarin at reducing strokes.
What monitoring do I need?	Once stabilised on warfarin patients need regular blood tests. Initially this will be one a week or fortnight and gradually increase to about once every six-twelve weeks when stabilised.	A blood test will be taken prior to starting and then you will need at least 1-2 more blood tests per year to ensure it remains safe to continue. Patients whose kidneys work less well may need more frequent tests.			
What is the risk of bleeding with this treatment?	All are anticoagulants - medicines made to stop blood from clotting rapidly. They are therefore all associated with an increased risk of bleeding. Major bleeding may be life threatening, particularly when the brain or gut is the cause of the bleeding. The risk of bleeding into the brain (a type of stroke) is less common with newer medicines than warfarin but the risk of bleeding from the gut is greater.				
	Risk of major bleeding each year with warfarin: 36 in every 1000 patients	Risk of major bleeding each year with dabigatran 150mg: 33 in every 1000 Risk of major bleeding each year with dabigatran 110mg: 29 in every 1000, this is less than with warfarin	Risk of major bleeding each year with rivaroxaban: 36 in every 1000 patients. In the clinical study with warfarin, slightly fewer patients on warfarin (34 in every 1000) had a major bleed	Risk of major bleeding each year with apixaban is 22 in every 1000 patients, this is less than with warfarin	Risk of major bleeding each year with edoxaban is 28 in every 1000 patients. This was less than with warfarin
	Dabigatran, rivaroxaban, edoxaban and apixaban have not been looked at together in one clinical trial so we cannot say which is better and because the studies were not exactly the same, the stroke risk and bleeding risk are not directly comparable.				
Long term safety	Long-term safety based on 60 years use in clinical practice.	No information available on long-term safety as fairly new			

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Is there an antidote?	An effective, readily available antidote is available, should there be too much warfarin in the body, a severe bleed occur or an urgent need for a major operation whilst being treated. The effects of warfarin can be reversed within 20 minutes and the effect can be accurately measured by blood tests.	There is a specific antidote to reverse the effects of dabigatran. It is kept at Hull and East Yorkshire Hospitals NHS Trust and other hospitals.	No true antidotes are currently available. Should a severe bleed occur or an urgent need for a major operation whilst being treated, donated human blood products (the same as those used to reverse warfarin) may help but may take some hours to achieve. These new anticoagulants, though, only stay in the body for a short period and if they are stopped clotting factors will be restored to their usual level naturally.		
Common Side Effects	<p>Though rashes, nausea (feeling sick), hair loss and diarrhoea are said to occur in practice few patients have problems with side effects.</p> <p>Bleeding including nose bleeds, bruising, vomiting blood and gastrointestinal (gut) bleeding can occur with warfarin, which can be an indication there is too much warfarin in your body and the blood tests can check this.</p>	Side effects affecting between 1 in 10 to 1 in 100 patients: nose bleeds, gastrointestinal (gut) bleeding, abdominal pain, diarrhoea, dyspepsia (heartburn), nausea (feeling sick), blood test abnormalities (anaemia, liver function changes)	Side effects affecting between 1 in 10 to 1 in 100 patients: Dizziness, headache, syncope (feeling faint) abdominal pain, gastrointestinal (gut) bleeding, dyspepsia (heartburn), nausea, constipation, diarrhoea, vomiting rashes, nose bleeds, minor eye bleeds (sub-conjunctival) blood test abnormalities (anaemia, liver function changes), tachycardia (palpitations), haematuria (blood in urine), menorrhagia (heavy periods)	Side effects which affect between 1 in 10 are eye haemorrhage, other haemorrhage (includes gums, gut and rectum), bruising and nose bleeds	Side effects affecting between 1 in 10 to 1 in 100 patients: Nausea, abnormal blood test (liver, anaemia), rash Itching, bleedings (gastrointestinal–gut, oral, skin, vaginal–menorrhagia, urine–haematuria and nose
	In the clinical study which compared warfarin and dabigatran in patients with AF, <i>more patients stopped treatment with dabigatran</i> than warfarin for reasons such as adverse side effects				
Compliance aids (devices to help you remember to take your medicines, e.g. dosset boxes)	Warfarin is not recommended to be put in compliance aids because the dose varies depending on the results of blood tests.	Capsules of dabigatran should not be put in compliance aids because the capsules are sensitive to moisture. There is a special compliance device which can be used with dabigatran	There are no concerns with them being placed in a compliance aid.		
Crushable and/or put through NG tube	Yes	No	Yes	Yes	Yes

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Interactions - when something else, like another medicine, food or alcohol affects the way a drug should work					
Drug-food interactions	Some foods interact with warfarin (e.g. foods containing high amounts of Vitamin K). Many vegetables such as broccoli, brussels sprouts and cabbage contain Vitamin K, so does liver and green tea. You do not have to stop eating these but should not suddenly increase or decrease the amount you eat.	Currently there are no known food interactions.			
Drug-drug interactions	Warfarin interacts with a number of drugs including antibiotics, epilepsy drugs, antifungals and <i>St John's Wort</i> . Some medicine interactions may mean that patients require extra monitoring and dose adjustment to ensure an appropriate effect. You should check with your GP whether any other medication you are taking interacts with warfarin	Some drugs can increase the effects of dabigatran (antifungals or immune suppressing drugs) and others reduce dabigatran effects (epilepsy drugs or <i>St John's Wort</i>), discuss with your GP.	Rivaroxaban interacts with certain other drugs that are processed by important CYP enzymes in the liver e.g. antifungals, antiepileptics or <i>St John's Wort</i>), discuss with your GP.	Apixaban interacts with certain other drugs that are processed by important CYP enzymes in the liver e.g. antifungals, antiepileptics or <i>St John's Wort</i>), discuss with your GP.	Edoxaban interacts with certain other drugs that are processed by important CYP enzymes in the liver e.g. antifungals, antiepileptics or <i>St John's Wort</i>), discuss with your GP.
Summary	Long-term safety based on 60 years use in clinical practice. Safe, used in millions of patients. Not expensive for NHS. Easily reversed Requires regular INR blood tests	New drug. Long term safety not known Requires some blood tests Expensive for NHS Easily reversed No INR blood tests needed	New drug. Long term safety not known Requires some blood tests Not easily reversed No INR blood tests needed	Requires some blood tests	Expensive for NHS

The pharmaceutical manufacturers of the direct oral anticoagulants (dabigatran, rivaroxaban, apixaban and edoxaban) have not signed up to the All Trials Petition. This seeks to ensure that ALL clinical trials are registered and have their results reported (good or bad).

Further detailed information is available at www.medicines.org.uk

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