

Patient / Healthcare Professional Decision Aid : ATRIAL FIBRILLATION Medicines to help reduce your risk of a stroke – What are the options?

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 oldest anticoagulant is warfarin. It has been used to prevent strokes in millions of people. There are now some new anticoagulant drugs: dabigatran (Pradaxa), apixaban (Eliquis), edoxaban (Lixiana) and rivaroxaban (Xarelto).

If your doctors consider that an anticoagulant is the best treatment for your condition the information in this leaflet should help you learn about the risks and benefits of each treatment to ensure you choose the 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, apixaban, edoxaban and rivaroxaban is only considered when an individual is diagnosed with 'non-valvular atrial fibrillation'.

What is my risk of having a stroke?

Your healthcare professional can use a risk score to estimate your risk of having a stroke (called the CHA₂DS₂-VASc) and risk of bleeding (called the HAS-BLED). The risk scores are based on factors such as your age and whether you have other medical conditions. The higher the score, the more likely it is that you will have either a stroke or major bleeding. However, it is important to remember that:

- No one can tell what will happen to an individual
- Even if your score on either system are low or zero, you might still have a stroke or major bleeding
- If your scores are high it does not mean that you will definitely have a stroke or mayor bleeding
- Taking anticoagulation will save some people having a stroke caused by AF, but some people will still have a stroke even though they take the anticoagulant.
- Although taking an anticoagulant increases the risk of major bleeding, this will not happen to many taking this medicine; some people will have major bleeding even if they don't take an anticoagulant.

Stroke and bleeding risk scoring systems

CHA ₂ DS ₂ -VASc score	
Risk factor	Score (Circle)
Congestive heart failure or left ventricular dysfunction	1
Hypertension	1
Age 75 years or greater	2
Age 65–74 years	1
Diabetes mellitus	1
Stroke, transient ischaemic attack or thromboembolism	2
Vascular disease (prior MI, peripheral artery disease)	1
Sex category (female)	1
Total	

HAS-BLED score	
Risk factor	Score (Circle)
Hypertension (uncontrolled)	1
Abnormal liver function (bilirubin 2x ULN)	1
Abnormal renal function (creatinine over 200)	1
Stroke	1
Bleeding (previous bleeding history)	1
Labile INR	1
Elderly (over 65, frail)	1
Drugs (antiplatelets/NSAIDs)	1
Alcohol abuse	1
Total	

Once your healthcare professional has calculated your score they can discuss the benefits and risks of anticoagulant treatment. National Institute for Health and Care Excellence (NICE) Patient decision aid shows this information in graphs.

www.nice.org.uk/guidance/cg180/resources/patient-decision-aid-243734797 . A summary of their information is below.

CHA ₂ DS ₂ -VASc score	1000 patients with no treatment for one year.	1000 patients with anticoagulant for one year		
	How many will have a stroke?	People who have a stroke anyway	People saved from having a stroke	People who wouldn't have a stroke anyway
1	6	2	4	994
2	25	8	17	975
3	37	12	25	963
4	55	17	38	945
5	84	27	57	916

HAS-BLED score	1000 patients with no treatment for one year.	1000 patients with anticoagulant for one year		
	How many will have a major bleed?	People who have a major bleed anyway.	People who have a major bleed because of treatment.	People who do not have a major bleed
1	3	3	4	993
2	7	7	12	981
3	9	9	15	976
4	13	13	21	966

ATRIAL FIBRILLATION : Medicines to help reduce your risk of a stroke - What are the options?

This leaflet lists the key information about the available treatments for preventing a stroke in patients with Atrial Fibrillation (AF). They are all anticoagulants (medicines made to stop blood from clotting rapidly) and are therefore all associated with an increased risk of bleeding. It is your choice which medicine you take. Read through the information about the treatments and discuss it with your GP.

		Newer anticoagulant treatments : DAOCs : Direct acting oral anticoagulants			
Generic Name	Warfarin	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
Brand Name	Marevan	Pradaxa	Eliquis	Lixiana ▼	Xarelto ▼
Date of first authorisation	1950s	2013 in UK for AF	2011 in UK for AF	2015 in UK for AF	2011 in UK for AF
Black Triangle ▼	A black triangle indicates a new medicine or one that is being used to treat new condition and is 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. Warfarin has long-term safety established based on 60 years use in clinical practice. There is no information available on long-term safety of DOACs yet as they are relatively new.				
	No	No	No	Yes	Yes
Strength of pills available	0.5mg, 1mg, 3mg and 5mg	150mg or 110mg	2.5mg or 5mg	60mg or 30mg or 15mg	20mg or 15mg
	The dose for each patient may alter with age, weight, kidney function, bleeding risk and other medications				
How to take it	ONCE daily The dose will be changed depending on INR blood test result.	TWICE daily	TWICE daily	ONCE daily	ONCE daily with food
What happens if I forget to take a dose?	You should take warfarin as prescribed at the same time every day. If you think you may have missed a dose you should take it as soon as you remember, but do not take two doses in one day. The protective effect against strokes does not wear off as quickly as with DOACs.	It is important to take these tablets as prescribed. If you forget a dose the protective effect of a DOAC on the risk of a stroke may fade 12 – 24 hours after you take a dose.			
		May still be taken up to 6 hours before the next dose. From 6 hours before the next dose, the missed dose should be missed. No double dose should be taken to make up for missed individual doses.	Take immediately and then continue with twice daily intake as before.	Take immediately and continue the following day with the once daily dose as recommended. The dose should not be doubled within the same day to make up for a missed dose.	Take immediately and continue the following day with the once daily dose as recommended. The dose should not be doubled within the same day to make up for a missed dose.

Newer anticoagulant treatments : DAOCs : Direct acting oral anticoagulants

Generic Name	Warfarin	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
What monitoring do I need?	Patients on warfarin need regular INR blood tests. Initially this will be once a week and gradually increased to about once every four weeks. The maximum interval is twelve weeks when stabilised.	Blood tests will be taken prior to starting and then you will need at least one or two more blood tests per year to ensure it remains safe to continue. Patients whose kidneys work less well may need more frequent tests. No INR blood tests are needed for patients on DOACs.			
Will it reduce my risk of having a stroke? Without treatment, out of 1000 patients with AF, <i>each year</i> we expect 40-50 patients to have a stroke.	In clinical trials each DOAC was compared to warfarin. DOACs 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.				
	Warfarin reduces the risk of stroke down to about 16 a year.	Dabigatran 150mg reduces the risk of a stroke down to about 11 a year. It was superior to warfarin at reducing strokes. Dabigatran 110mg reduces the risk of a stroke down to about 13 a year. This was as effective as warfarin at reducing strokes.	Apixaban reduces the risk of stroke down to about 13 patients a year. In clinical trials apixaban was superior to warfarin at reducing strokes.	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.	Rivaroxaban reduces the risk of stroke down to about 17 patients a year. In clinical trials rivaroxaban was as effective as warfarin at reducing strokes.
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 if the brain or gut is involved. The risk of bleeding into the brain (a type of stroke) is less common with DOACs than warfarin. The risk of bleeding from the gut is greater for dabigatran, edoxaban and rivaroxaban than for warfarin or apixaban.				
	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 patients. This was comparable with warfarin. Risk of major bleeding each year with dabigatran 110mg: 29 in every 1000 patients. This was less than with warfarin	Risk of major bleeding each year with apixaban is 21 in every 1000 patients. This was less than with warfarin	Risk of major bleeding each year with edoxaban is 28 in every 1000 patients. This was less than with warfarin	Risk of major bleeding each year with rivaroxaban is 36 in every 1000 patients. This was comparable with warfarin.
Is there an antidote?	There are well established treatments to reverse the effects of warfarin	There is a specific antidote to reverse the effects of dabigatran. It is kept at both York & Scarborough hospitals.	No true antidotes are currently available, though DOACs only stay in the body for a short period and if they are stopped clotting factors will be restored to their usual level naturally. If necessary donated human blood products (the same as those used to reverse warfarin) will be given and other supportive measures used.		

Newer anticoagulant treatments : DAOCs : Direct acting oral anticoagulants

Generic Name	Warfarin	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
Common Side Effects (1 in 10 to 1 in 100 patients)	Rashes Nausea (feeling sick) Hair loss Diarrhoea <u>Bleeding</u> Bruising Nose bleeds	Nausea (feeling sick) Dyspepsia (heartburn) Diarrhoea Abdominal pain Abnormal blood test (liver, anaemia) <u>Bleeding</u> Gastrointestinal –gut Nose (epistaxis) Skin Urine (Haematuria)	<u>Bleeding</u> Eye Gastrointestinal –gut Rectal Nose Skin (bruising) Urine (haematuria)	Nausea Abnormal blood test (liver, anaemia) rash itching <u>Bleeding</u> Gastrointestinal –gut Oral Skin Vaginal (menorrhagia) Urine (haematuria) Nose	Dizziness Headache Abdominal pain Dyspepsia (heartburn) Nausea/Vomiting Constipation/Diarrhoea Rashes / itching Abnormal blood tests (liver, anaemia) <u>Bleeding</u> Gastrointestinal –gut / rectal Eye Nose / gums Coughing up blood (haemoptysis) Menorrhagia (heavy periods, Urine (haematuria) Skin

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, brussel sprouts and cabbage contain Vitamin K, so does liver and green tea. You do not have to stop eating these but should not suddenly change the amount you eat.	Currently there are no known food interactions with DOACs
Drug-alcohol interactions	High alcohol intake can alter the results of the INR blood test. You should follow national guidelines on how much is safe to drink and never binge drink.	Currently there are no known interactions with alcohol and DOACs (however, you should still follow national guidelines on how much is safe to drink).

Newer anticoagulant treatments : DAOCs : Direct acting oral anticoagulants					
Generic Name	Warfarin	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
Drug-drug interactions	Warfarin can interact with several medicines, including antibiotics, those bought over the counter and herbal medicines. It is important to ask advice of your health professional before starting and stopping any medicines. You may need extra INR blood tests with some medications.	<p>There are fewer drug interactions with DOACs than with warfarin.</p> <p>Some drugs can increase their effects (antifungals or immune suppressing drugs) and others reduce them (epilepsy drugs or <i>St Johns Wort</i>), discuss with your GP or health professional before starting or stopping any medicines. Edoxaban interacts with the antibiotic erythromycin and the edoxaban dose should be halved while taking it.</p>			
Compliance aids (devices to help you remember to take your medicines eg dosset boxes)	Warfarin is not recommended to be put in compliance aids because the dose varies depending on the INR blood test results	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	Apixaban, edoxaban and rivaroxaban have not been tested in blister packs but are stable out of the original packs. There are no theoretical concerns with them being placed in a compliance aid.		
Summary	Long established drug Used in millions of patients Can interact with food and alcohol Requires regular INR blood tests	New drug Clinical trials show the 150mg dose is more effective than warfarin with similar rates of major bleeding but less intracranial haemorrhage (brain bleed).It showed more gastrointestinal (gut) bleeding Clinical trials show the 110mg dose is as effective as warfarin with lower rates of major bleeding and less intracranial haemorrhage (brain bleed) No food & alcohol interactions No INR blood tests needed	New drug Clinical trials show it is more effective than warfarin with lower rates of major bleeding and less intracranial haemorrhage (brain bleed) No food & alcohol interactions No INR blood tests needed	New drug Clinical trials show it is as effective as warfarin with lower rates of major bleeding and less intracranial haemorrhage (brain bleed) It showed more gastrointestinal (gut) bleeding No food & alcohol interactions No INR blood tests needed	New drug Clinical trials show it is as effective as warfarin with similar rates of major bleeding but less intracranial haemorrhage (brain bleed) It showed more gastrointestinal (gut) bleeding No food & alcohol interactions No INR blood tests needed

References

Summary of Product Characteristics (Accessed July 2015)

Nice Guidelines; AF; Technology appraisals for dabigatran, apixaban, edoxaban & rivaroxaban

Nice Guidelines 2014 : AF Patient decision aid

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

XXXXX – dosette box info

Sources of further Information:

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

- The Atrial Fibrillation Association

AF Association

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Website www.atrialfibrillation.org.uk

- National Institute for Health and Care Excellence

NICE AF Patient decision aid

Website: www.nice.org.uk/guidance/cg180/resources/patient-decision-aid-243734797

- British Heart Foundation

Website www.bhf.org.uk

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