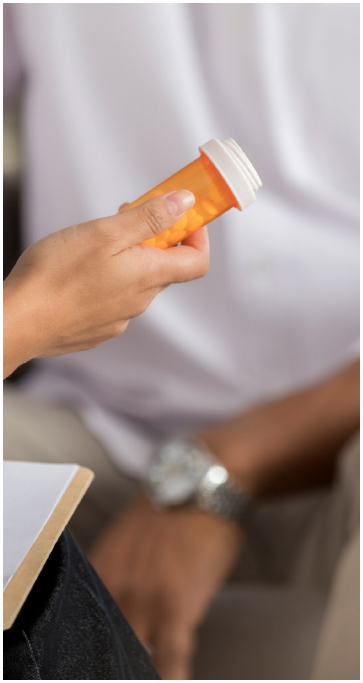
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Atrial fibrillation (AF) drug information







Working to provide information, support and access to established, new or innovative treatments for Atrial Fibrillation (AF)

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Glossary

Antiarrhythmic drugs Medication used to restore or maintain the normal heart rhythm

Anticoagulants Medication which helps to slow down the clotting process in blood

Arrhythmia Heart rhythm disorder

Atrial fibrillation (AF) Irregular heart rhythm caused by chaotic rhythm in the atria (top chambers of the heart)

Atrial excitability The ability of the cell to respond to an electrical impulse

Beta-adrenoreceptor Specialised receptors on heart cells that play an important role in the regulation of heart function including heart rate and contractability

Cardiologist A doctor who has specialised in the diagnosis and treatment of patients with a heart condition

Catheter ablation A treatment which destroys a very small (microscopic) area of tissue inside the heart which is causing an arrhythmia

Contraindication A specific situation in which a drug or procedure should not be used because it may **be harmful to the person**

Electrophysiologist (EP) A cardiologist who specialises in heart rhythm disorders

Half-life The time required for the activity of a substance taken into the body to lose one half its initial effectiveness

Sinus rhythm Normal regular heart rhythm

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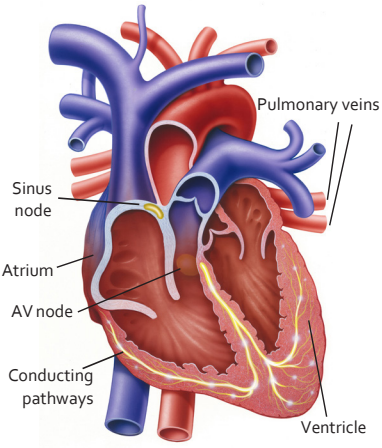
Anticoagulants

Transcatheter closure of the left atrial appendage

What is atrial fibrillation (AF)?

Atrial fibrillation (AF) is the most common heart rhythm disturbance (arrhythmia). It is a condition that is more common with advancing age, and if untreated can lead to serious complications, such as heart failure and stroke. It is estimated that more than one million people in the UK are living with AF.

AF occurs when chaotic electrical activity develops in the atria, and completely takes over the sinus node. As a result, the atria no longer beats in an organised way, and pump less efficiently. The AV node (a specialised cluster of heart cells) will stop some of these very rapid impulses from travelling to the ventricles, but the ventricles will still beat irregularly and possibly rapidly. This may contribute to symptoms of palpitations, shortness of breath, chest discomfort, light headedness, fainting or fatigue. The goal of treatment in AF is to restore the heart's normal rhythm and if this is not possible, then to slow the irregular heart rate, to alleviate symptoms and prevent complications of AF-related stroke and heart failure.



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Drug treatments for AF

Commonly the initial treatment of AF is with drug therapy. Other non-drug therapies, such as cardioversion, ablation and pacemakers, are generally used for AF patients whose quality of life is affected by AF or where drug therapies have failed. It is best to discuss the available treatment options with your doctor. The drugs used to restore the normal heart rhythm are known as antiarrhythmic drugs. They work by blocking specific electrical conduction channels in the heart. Some drugs slow the activation of the heart muscle, and others slow the recovery of the heart muscle. Drugs of a certain class are effective for particular rhythm disturbances, so your doctor will make an assessment based upon your symptoms and the details of your diagnosis.

Although different classifications schemes have been proposed for antiarrhythmic drugs, the one that most physicians use is the Vaughan-Williams classification. This describes seven different classes of antiarrhythmic drugs (Table 1).

Table 1:

The 'Vaughan-Williams' classification for antiarrhythmic drugs

Class	Kind of drug	Examples
Ia	Sodium channel blockers	Disopyramide
Ib	Sodium channel blockers	Lidocaine, mexiletine
Ic	Sodium channel blockers	Flecainide, propafenone
II	Beta blockers	Bisoprolol, atenolol
III	Potassium channel blockers	Sotalol, amiodarone
IV	Calcium channel blockers	Verapamil, diltiazem
V	Direct nodal inhibitors	Digoxin

Rhythm or rate control

A rhythm control strategy aims to use medication to return the heart to its normal rhythm. It is a major goal of AF management, because symptoms can be relieved, and the risk of stroke and other complications can possibly be reduced, but not eliminated. A number of drugs are available to restore the normal heart rhythm. Sometimes your doctor might decide to accept that rhythm control drugs will not work. In this case the doctor will use antiarrhythmic drugs to control your heart rate from going too high. Drugs are usually effective with either rhythm control or rate control but have side effects, so they need to be monitored. Ask your doctor if you have any concerns prior to commencing treatment.

Class I drugs work by blocking the sodium channel in the cardiac cell.

- **Class IA** drugs are called membrane stabilising agents which decrease excitability of the heart cells. The action potential is lengthened by class Ia agents. Dysopyramide is still used for some forms of AF.
- **Class IB** drugs are not commonly used in AF, because they are rarely effective. They lengthen the duration of the action potential, thus decreasing the heart rate.
- **Class IC** drugs are commonly used to treat AF and are very effective. They are used in patients with no history of a previous heart attack and normal heart function. These include flecainide and propafenone. However, rare side effects include unstable cardiac rhythms or excessive slowing of the heart rate. They are generally reserved for younger patients with AF and no structural heart disease. Patients taking these drugs should be monitored carefully by their doctor.

Class II drugs or beta blockers are commonly used to slow the heart rate and are effective in active patients. These include bisoprolol, atenolol, metoprolol, etc. They act by blocking the effects of adrenaline and other similar hormones, thereby decreasing sympathetic activity on the heart. They can only be used with great care in patients with asthma or emphysema and in patients with slow heart rates. Patients taking these medications will need their blood pressure and heart rate checked regularly by their family doctor or GP. The most commonly reported side effect is tiredness. Beta blockers will also stunt your heart rate response to exercise. You should be aware of this if you monitor your heart rate during exercise.

Class III drugs work mostly by blocking the potassium channel in the cardiac cell. These drugs include sotalol and amiodarone. Sotalol is also a beta blocker and slows the heart rate, but at higher doses can act to stabilise the heart rhythm. The main side effects are related to slow heart rate and low blood pressure, causing symptoms of tiredness or fatigue, dizziness or fainting.

Sotalol can be dangerous if a patient has an illness with diarrhoea and vomiting. Sotalol should not be used if potassium losing diuretics are prescribed. Studies have shown amiodarone to be one of the most effective antiarrhythmic drugs. It is also safe to use in the elderly and in patients with underlying heart conditions. Amiodarone has many side effects (pulmonary fibrosis, thyroid abnormalities, corneal deposits, abnormal liver function tests, and skin sensitivities) so needs regular monitoring by health care specialists.

Class IV drugs

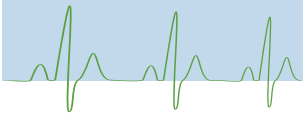
Verapamil and diltiazem are class IV drugs which also slow the heart rate. They have to be used with caution in patients with heart failure. Adverse side effects relate to flushing, headaches, low blood pressure and ankle swelling. Any adverse side effects should be reported to your doctor immediately. Patients taking these medications should have their blood pressure and heart rate checked by their doctor. Combinations of beta blockers and calcium channel blockers can only be used with great care, bearing in mind the underlying heart pumping function. Diltiazem is a calcium channel blocker which acts by interfering

Rate control for AF

Rate control refers to slowing the irregular heart rate without attempting to restore the normal heart rhythm.

Rate control is not inferior to rhythm control and is an attractive alternative in patients with a high risk of AF recurrence.

Drugs used to slow the heart rate aim to improve symptoms and prevent the effects of an uncontrolled irregular fast heart beat.



with calcium in the heart cells. It is by affecting the cell's calcium channels which influences the heart's electrical activity. The tablets can come in a huge variety of doses and types (slow-release/ modified release/retard/long-acting).

Class V drugs

In less active patients, digoxin can be used. Digoxin decreases conduction of electrical impulses through the AV node and increases vagal activity on the AV node leading to an overall decrease in speed of conduction. The result is a decrease in heart rate. Combinations of digoxin and beta blockers may be required to achieve effective rate control. However, given its ineffectiveness during activity, it is not routinely used for rate control.

Rate vs rhythm

Unfortunately, there is no 'one size fits all' answer to the management of AF. Multiple drugs may be tried and adjusted until one is found that achieves the desired goal of optimal rate or rhythm control with minimal side effects. Physicians and patients must tailor the choice of drug to each individual. All drugs have the potential to cause side effects.

It is important to consult your physician if you experience any side effects related to your treatment and to have regular follow up to check your blood pressure, heart rate, ECG and any blood tests required to monitor progress. Exercise testing or ambulatory ECG monitoring may be used to check the quality of rate control.

Flecainide

Flecainide slows conduction in cardiac cells decreasing their excitability; preventing and sometimes terminating AF. It also slows conduction in the accessory pathways responsible for the Wolff-Parkinson-White (WPW) syndrome that can be associated with AF. Flecainide is especially useful in patients with paroxysmal AF where there is no structural or coronary heart disease.

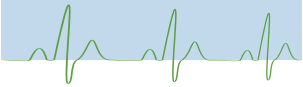
Flecainide can sometimes organise AF into a fast and regular rhythm called atrial flutter; this may lead to a fast heart rate in some cases, so flecainide is often combined with a drug to slow the heart rate down just in case.

Flecainide is metabolised in the liver with a half-life of around 14 hours so it is usually administered twice daily. In some patients with heart disease and in those with poor kidney function it can accumulate so dose reductions may be needed. Flecainide may be used in pregnancy following appropriate discussions and after consideration of other approaches.

Contraindications: Flecainide has a variable half-life and often causes QRS prolongation (signifies a delay in the contraction of the ventricles of the heart) and PR prolongation (indicates delayed conduction of the heart beat from the atria to the ventricles) on the ECG. The British National Formulary recommends that flecainide is only given on the advice of a hospital consultant. Flecainide is contraindicated in patients with sinus node disease, atrioventricular block or bradycardia (without pacemaker support) and it should also be used with caution in those who have received pacemakers.

Side effects: Adverse side effects are usually temporary and can include, nausea, blurred vision, dizziness, constipation, diarrhoea and headaches.

Occasionally flecainide may cause shortness of breath, skin irritation and chest pains. If you are concerned that flecainide is causing any problems, it is important to seek medical advice promptly.



Beta blockers

These are used widely in cardiology not just for their excellent antiarrhythmic effects, but also following heart attacks and in heart failure patients.

Beta blockers block beta-adrenoceptor receptors in the heart, peripheral vessels, and lungs. Beta blockers like bisoprolol are cardio-selective which mean they specifically target the receptors in the heart.

In those with a history of asthma, beta blockers should not be used unless under specialised supervision; however in patients with longstanding lung disease (COPD), a beta blocker like bisoprolol can be initiated under specialised supervision. If breathing becomes worse or a cough develops then the beta blocker should be stopped.

Those with peripheral vascular disease might also find there is reduced blood flow to the legs and experience cold feet. Therefore, a decision to start a beta blocker would be with specialised supervision.

Diabetics can use beta blockers, but care should be taken as beta blockers can affect carbohydrate metabolism masking symptoms of a hypoglycaemic attack.

Beta blockers also stunt the heart rate response to exercise, so if you monitor your heart rate during exercise, you will probably not be able to get to higher heart rates you did before you started taking the medication.

Common side effects of beta blockers, specifically bisoprolol, can include: dizziness, weakness, drowsiness or fatigue and shortness of breath. There will be a list of side effects in your medication packet which you should read thoroughly before commencing.

Sotalol

Sotalol is a beta blocker and as such is probably effective because it counteracts the arrhythmogenic effect of adrenaline and similar influences that may trigger attacks of AF. Sotalol has other actions to make the atrial cells less excitable through blocking potassium channels, but only at relatively high doses and side effects are common. This second action is beneficial in the atria but may have adverse effects on the ventricle so the dose of sotalol should be increased with caution and with periodic ECG monitoring.

Cautions: By prolonging the recovery phase of the heart beat cycle, sotalol can predispose to ventricular arrhythmias (a form called 'Torsades de pointes') that can be risky, and may be life-threatening if there is a situation with low potassium and low magnesium levels, as with diarrhoea and vomiting. To minimise the likelihood of this problem if there is evidence of renal impairment the dose needs review and reduction. Potassium losing diuretics should not be taken in combination with sotalol.

Side effects: The main side effects from beta blockers in general are due to slowing of the heart and depression of the contraction of the heart. Accordingly an unduly slow pulse (bradycardia) or symptoms of heart failure can result in other effects including fatigue, sleep disturbance, shortness of breath, sexual dysfunction and depression.

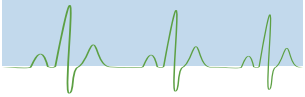
Interactions: Associated intravenous administration of a calcium channel blocker (verapamil, diltiazem), that affects conduction, increases the risk of bradycardia and should in general be avoided.

Propafenone

Propafenone has many of the same actions as flecainide and the precautions and contraindications regarding its use are almost identical.

It has the subsidiary action of blocking β-receptors with an action equivalent to a low dose of sotalol. The liver metabolises it and side effects are similar to those of flecainide and are more common in poor metabolizers of the drug.

In general in the UK it tends to be chosen as an alternative, for example if flecainide or sotalol have proven useful and/or effective but have not been tolerated.



Dronedarone

Dronedarone is similar to amiodarone in structure, but has modifications to make its metabolism faster and reduce the chance of thyroid problems. Its main mechanism of action is inhibition of potassium channels leading to a decrease in atrial excitability. It has been shown to be effective in reducing the risk of AF recurrence by 25% and has also been shown to reduce ventricular response rates. A large randomised clinical trial has demonstrated that dronedarone reduces hospitalisations in AF.

Dronedarone should be initiated and monitored by an appropriate hospital consultant or specialist nurse practitioner.

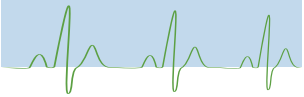
Contraindications: An increased incidence of heart failure has been seen with exposure to this drug, therefore dronedarone should not be prescribed to patients with heart failure or impaired heart function and the patient should be regularly reviewed. Dronedarone should also be avoided in patients with significant liver disorders and frequent liver function tests (blood samples) are needed during the initial period of treatment.

Guidance on monitoring has been issued by the Medicines and Healthcare products Regulatory Agency. Patients with heart block, or sick sinus syndrome (unless used in conjunction with a functioning pacemaker), or corrected QT interval >500ms should not be given dronedarone.

Side effects:
Dronedarone is generally well tolerated but common side effects are diarrhoea, abdominal discomfort, nausea and vomiting.

There is an increased incidence of skin rash, bradycardia and prolonged QT interval although Torsades de pointes is very rare.

Most side effects resolve within the first two weeks after drug commencement but in a proportion of patients, dronedarone may need to be discontinued because of intolerance.



Amiodarone

Amiodarone is used to help keep the heart in its normal (sinus) rhythm. It is often used if previous cardioversions have failed and your doctor is attempting to get your heart back to normal rhythm with cardioversion. It can sometimes be used prior to an AF ablation to help increase the chances of success. It is also used when the heart has changed its rhythm (arrhythmia) to help it return to normal rhythm. Amiodarone has a low risk of proarrhythmia and is commonly used in patients with structural heart disease. Sometimes it is necessary to 'load' amiodarone with high doses initially and then reduce to a lower maintenance dose. It takes a number of weeks before amiodarone is fully loaded into the body. Likewise it will take a number of weeks for amiodarone to completely be out of the body. Doctors are careful who they start amiodarone on for this reason.

Side effects

Amiodarone is the most effective antiarrhythmic drug available and although generally well tolerated, amiodarone does have side effects that can affect many different parts of the body.

Skin: Photosensitivity can occur, meaning when the skin is exposed to sunlight, it can turn red, resembling severe sunburn! Whilst this is not harmful, it is cosmetically undesirable to most patients. Furthermore, over time the skin can become a slate-grey colour. Thus we normally recommend that a sun screen is used, or a hat and/or clothing.

Thyroid gland: The thyroid gland produces a hormone which controls the body's metabolism. Amiodarone can affect this gland making it both overactive (this occurs in about two percent of people taking amiodarone) or underactive (this occurs in about six percent of people taking amiodarone). Your doctor will take regular blood tests to check if either of these has developed. Both an overactive and underactive thyroid can be treated with medicines.

Eyes: Small deposits can form in the cornea of the eye (the clear surface that covers the pupil, iris and white of the eye). These deposits are not harmful. However, you may notice the effect of these eye deposits if looking at bright

lights at night, for example when driving a car. One in ten people taking amiodarone will experience a bluish halo in their vision. Again this is not harmful.

Lungs: Amiodarone can cause problems with thickening (fibrosis) of the structures of the lungs. If you feel you have problems with shortness of breath then you should arrange to see your GP straight away.

Liver: On rare occasions amiodarone causes problems with the function of the liver. Your doctor will check for any effect on the liver by doing routine blood tests every six months.

Monitoring

Amiodarone is a very useful medication and will only have been commenced in your clinical best interest. The side effects listed above, mean that monitoring is important.

You will need to be reviewed by your GP every six months whilst on amiodarone. They will arrange blood tests for thyroid and liver function, and review any other problems.

Digoxin

Digoxin is a medication commonly used in the treatment of AF and atrial flutter. In some people with heart failure (where the main pumping chamber, the left ventricle, loses its strength) it can be used to increase the force of contraction to assist with improving a patient's symptoms.

Dosing: Initially this may be taken twice daily to load the body and boost its effectiveness, and after that is usually prescribed as a once daily medication.

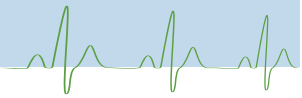
Monitoring: Digoxin is a safe medication for long term use. It is always advisable to have regular check-ups while on the medication and this may be done once or twice a year. Generally the effects of digoxin can be monitored through a physical examination (taking the pulse and blood pressure).

Occasionally the doctor may ask for a blood test to be performed to check the level of digoxin in the blood, although this is not routine practice.

Side effects: Digoxin is a medication which can present with signs of toxicity (high levels of digoxin in the blood even though the dose taken has remained unchanged).

The symptoms of toxicity include loss of appetite, nausea, vomiting, diarrhoea, blurred vision, visual disturbances (yellowgreen halos around people or objects, some people describe these as auras), confusion, drowsiness, dizziness, nightmares, and agitation.

If you are concerned that digoxin is causing any problems it is important to seek medical advice promptly.



Other medication

AF may occur in association with other disorders (but by no means always), so you may be taking a number of drugs. These drugs are necessary, so must be continued, however you must inform each doctor you see of all the drugs you are currently taking. Always remember to take your prescription or the original packets / boxes for ALL your tablets whenever you visit a nurse or doctor. This will help reduce mistakes in prescribing and helps when the doctors and nurses need to communicate about your treatment.

When taking a complicated 'cocktail' of drugs it can be hard to remember which tablets to take and when. It may be worth considering getting a tablet box which sets out all the tablets you need for the day or week, and helps you to take them correctly and on time. It is also wise to check your tablets every time you have a new prescription – mistakes can be made. Sometimes your tablets may look different because they have come from a different manufacturer (even though the drug is the same).

Medication for infrequent/paroxysmal AF

In some patients with infrequent or intermittent AF, a 'pill in the pocket' approach may be used so that patients can simply take a single dose of the drug when episodes occur. However, this approach is reserved for a select group of patients. The NICE guidelines recommend a 'pill in the pocket' strategy can be considered for those who:

i) have no history of cardiac or coronary disease,
ii) have a history of infrequent symptomatic episodes of AF,
iii) have a systolic blood pressure > 100 mmHg and a resting heart rate above 70 beats per minute,
iv) are able to understand how to, and when to take the medication.

You must consult your physician to discuss whether you may be suitable for this treatment option. Also, using the drug this way will not prevent episode of AF and the inconvenience caused by them. In addition, it will not affect the natural history of AF which is of more frequent, longer-lasting attacks leading to persistent AF. Please see AF Association's Pill in the pocket factsheet.

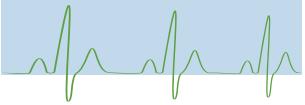
What should I do if I feel really ill with my tablets?

Contact your physician BEFORE stopping any medication, as sudden cessation of treatment can sometimes result in an unpleasant return of your AF, perhaps worse than before treatment. Your doctor will arrange to see you or give advice about what to do. If you feel too unwell to contact your GP, you should consider visiting A&E, taking all of your medication with you.

Some medication used to control AF stays in the body long after you may have stopped using the medication; and side effects take a while to diminish. Amiodarone (Cordarone X) often causes this problem; it takes many weeks to reach stable levels in the body and takes at least three months to be removed from your body once stopped. This means that changes in dose will take some time to take effect as well as side effects continuing for some time after stopping the drug. Most other drugs are not as persistent as this, but it may take several days for a change in dose to have effect.

DO NOT GET PREGNANT ON ANY OF THESE DRUGS

When drugs are tested, pregnant women are not enrolled in the studies. We simply do not know for many drugs what the effect would be to the baby. Therefore if you are trying to get pregnant, are pregnant, or are breast feeding, it is important that you consult a specialist.



IF IN DOUBT CONTACT YOUR GP, CARDIOLOGIST, ELECTROPHYSIOLOGIST OR ARRHYTHMIA NURSE.

How long will I take these tablets?

Unlike antibiotics or some other drugs, medication prescribed to control atrial fibrillation is not a 'course'; the drugs prescribed are intended to suppress, rather than cure, your AF. Therefore you should expect to continue these tablets indefinitely unless your GP/doctor changes them or recommends another form of treatment.

Remember that new treatments for AF are being studied all of the time, so there may be other options in the future.

What happens if these tablets do not work?

If your first drug does not work or results in intolerable side effects, there are others available and it may be that your GP/doctor will need to try several drugs before finding the right one for you. This is not trial and error – he/she will know the right type of drug to use, but predicting which one gives you least side effects whilst controlling your AF is rarely possible with an individual patient!

When suitable drugs have been tried, but have had limited or no success, your physician may consider alternative treatments. This may include cardioversion (only suitable with persistent atrial fibrillation) or catheter ablation, or possibly a pacemaker. Catheter ablation is a specialist treatment so it may be necessary for you to be referred to a specialist cardiologist called an electrophysiologist (EP), possibly at a different hospital. Your cardiologist will discuss this with you if the situation arises.

Anticoagulants



In AF the chaotic electrical activity means that the atria (top chambers of the heart) no longer contract together but instead the muscle quivers like a bag of worms. A lack of efficient contraction means the blood within the atria becomes stagnant and can form clots. These clots can travel anywhere in the body but most worryingly they can travel to the brain and cause a stroke. Indeed the risk of stroke in AF is five times greater than in the normal sinus rhythm (regular heart rhythm). This is why people with AF may need to have anticoagulants, to reduce the risk of clots forming and thus reduce the risk of strokes.

Antiplatelet drugs such as aspirin and clopidogrel, stop the activation of platelets. Although antiplatelet medication has been used for many years to prevent stroke, The National Institute for Health and Care Excellence (NICE) no longer recommends the use of aspirin for AF-related stroke prevention.

Anticoagulants act to stop the formation of fibrin, which is a long protein that binds together to form clots. In Britain, they currently include warfarin, dabigatran, rivaroxaban, apixaban, edoxaban and heparin.

The choice of which anticoagulant is best for you depends on:
(i) your personal risk of AF-related stroke
(ii) if any interventions such as cardioversion or ablation are planned
(iii) existing co-morbidities such as kidney impairment or heart valve disease

It is vital that you should discuss anticoagulation with your doctor who will calculate your individual AF-related stroke risk and prescribe an anticoagulant if appropriate.

For more information on anticoagulation, see 'Preventing AF-related stroke'

Notes

This booklet has been written to support those diagnosed with an arrhythmia and their carers, who struggle to find information on this condition. Without donations and fundraising, we would not be able to provide support through our award-winning resources and helpline.

Please donate to support our vital work at
www.heartrhythmalliance.org/afa/uk/get-involved/donate

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Arrhythmia Alliance

www.heartrhythmalliance.org

Working to provide information, support and access to established, new or innovative treatments for Atrial Fibrillation (AF)

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Registered Charity No. 1122442

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Published May 2008
Reviewed March 2025

endorsed by DH Department of Health

Affiliated to Arrhythmia Alliance

"This resource is a must for anyone taking medication for AF - it provides a well informed explanation even down to the side effects!"

William, Lincolnshire

To view our patient resources, scan the QR code below:

Please remember that this publication provides general guidelines only. Individuals should always discuss their condition with a healthcare professional. If you would like further information or would like to provide feedback, please contact AF Association.

Acknowledgments: AF Association would like to thank all those who helped in the development and review of this publication. Particular thanks are given to Dr Matthew Fay.

Founder and CEO:
Trudie Lobban MBE, FRCP (Edin)

If you would like further information or would like to provide feedback please contact AF Association.