



atrialfibrillationassociation
Australia

www.atrialfibrillation-au.org
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Providing information, support and access to
established, new or innovative treatments for Atrial Fibrillation

ATRIAL FIBRILLATION (AF) DRUG INFORMATION



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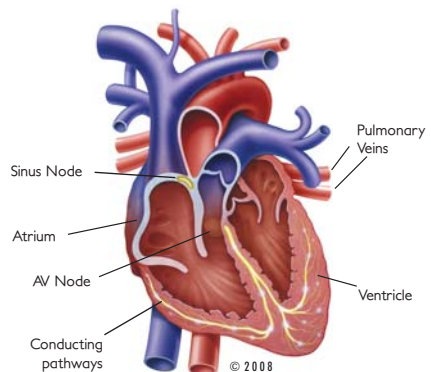
Anti-arrhythmic drugs	Drugs used to restore/maintain the normal heart rhythm
Anticoagulant	Drugs which help to thin the blood
Arrhythmia	Heart rhythm disorder
Arrhythmia Nurse Specialist	A nurse who is trained in heart rhythm disorders
Atrial Fibrillation (AF)	Irregular heart rhythm
Cardiologist	A doctor who has specialised in the diagnosis and treatment of patients with a heart condition
Catheter ablation	A treatment which destroys a very small area inside the heart causing the AF
Electrophysiologist (EP)	A cardiologist who has specialised in heart rhythm disorders
Sinus rhythm	Normal rhythm of the heart

What is Atrial Fibrillation?

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.

Atrial Fibrillation results from a disturbance in the normal electrical pathways in the heart (Figure 1). The normal pathway is interrupted by a disorganised electrical circuit which causes an irregular heart rhythm and sometimes a fast heart rate. This may cause 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, if this is not possible then to slow the irregular heart rate, to alleviate symptoms and prevent complications of AF related to stroke and heart failure.

The heart and normal conduction



Drug treatments for Atrial Fibrillation

The mainstay of treatment of AF is with drug therapies. Other non-drug therapies such as pacemakers and ablation therapies are generally used for certain AF patients who may not respond to drug treatments. It is best to discuss the available treatment options with your doctor. The drugs used to restore the normal heart rhythm are known as anti-arrhythmic drugs. They work by blocking specific channels in the heart. Anti-arrhythmic drugs fall into different drug classes because they work in differing ways. Some classes and even certain drugs within a class are effective for particular rhythm disturbances, so your doctor will make an assessment based upon your symptoms. Although different classifications schemes have been proposed for anti-arrhythmic drugs, the one that most physicians use is the Vaughan-Williams classification. This describes four different classes of anti-arrhythmic drugs - (Table1).

The Vaughan-Williams Classification for Anti-arrhythmics

Class I		
Sodium Channel Blocking Drugs Class 1A	Quinidine Procainamide Disopyramide	Moderately slow conduction moderately prolonged action potential duration
Class IB	Lidocaine Mexiletine Tocainide Phenytoin	Minimally slow conduction shortened action potential duration
Class IC	Flecainide Encainide Propafenone Moricizine	Markedly slow conduction minimally prolonged action potential duration
Class II		
Beta-blocking drugs	Bisoprolol Metoprolol Atenolol	
Class III		
Potassium-channel blocking drugs	Amiodarone Dronedarone Bretylium Sotalol	Prolonged action potential duration
Class IV		
Calcium-channel blocking drugs	Verapamil Diltazem	

Rhythm Control

A rhythm control strategy aims to use medication to return the heart to its normal rhythm. It is the main goal of AF management. A number of drugs are available to restore the normal heart rhythm. These drugs are effective but may have significant side effects, so they will need to be monitored for tolerability. Ask your doctor if you have any concerns prior to commencing treatment. Beta blockers (Class II drugs) are usually tried first, but they are not often successful. Class I and III drugs are typically reserved for rhythm control in AF.

Class I drugs work by blocking the sodium channel in the cardiac cell. Class IA drugs such as disopyramide and quinidine are effective in restoring and maintaining the normal rhythm but are limited in their use by their propensity to cause other troublesome rhythm problems. These side effects do not appear to be dose-dependent.

Class IB drugs such as lidocaine and phenytoin are not commonly used in AF. They are reserved for patients with underlying heart disease and rhythm disturbances other than AF.

Class IC drugs commonly used to stop AF include propafenone and flecainide. In patients with no history of coronary heart disease and normal heart function, these drugs are very effective in returning patients to the normal rhythm. Flecainide is usually taken twice daily whilst propafenone can be taken up to three times daily. However their side effects may include unstable cardiac rhythms, excessive slowing of the heart rate and heart failure. Hence, these drugs, whilst effective, are generally reserved for younger patients with AF and no structural heart disease. Patients taking these drugs should be monitored by their doctor.

Class III drugs work 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. It is taken twice or three times daily. The main side effects are related to slow heart rate and low blood pressure, causing symptoms of lethargy, dizziness and fainting. Amiodarone is considered one of the most effective anti-arrhythmic drugs in comparative studies. It is also safe to use in the elderly and in patients with underlying heart conditions.

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 as episodes occur. However, this approach is reserved for a select group of patients and must be tested in a hospital setting first to ensure safety, tolerability and efficacy. You must consult your physician to discuss whether you may be suitable for this treatment option.

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.

Class II drugs

Beta blockers are class II drugs commonly used to slow the heart rate and are effective in active patients with better exercise capacity. These include atenolol, metoprolol, bisoprolol etc. They are not recommended 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 local doctor.

Class IV drugs

Verapamil and Diltiazem are class IV drugs which also slow the heart rate. They are not suitable for patients with heart failure. Adverse effects relate to flushing, headaches, low blood pressure and ankle swelling. Pre-existing medical conditions and current medications should be discussed with your physician to establish whether any contraindications or drug interactions exist. Any adverse effects should be reported to your doctor immediately. Patients taking these medications should have their blood pressure and heart rate checked by their doctor.

Other rate control drugs

In less active patients, digoxin can be used. Combinations of digoxin and beta blockers may be required to achieve effective rate control. However, given its significant side effect profile, it is not routinely used for rate control. 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. 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.

Flecainide

Flecainide slows conduction in cardiac cells decreasing their excitability and both preventing and under some circumstances 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 in which case it must be used in conjunction with an agent such as a beta blocker or calcium channel blocker (verapamil or diltiazem) that slow the AV node to protect against rapid conduction to the ventricle. Such a situation can potentially arise if there are slowing and organization of the AF waves in the atria.

Flecainide is metabolized 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: Following observations made over 20 years ago in the CAST study flecainide is now restricted to patients without evidence of coronary or structural heart disease. It is also to be avoided in those with a history of myocardial infarction especially if they have a history of ventricular arrhythmia. It is also 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 effects that are usually minor and transient include blurred vision, abdominal discomfort, nausea, dizziness, tremor, abnormal taste sensations and paraesthesiae (tingling in the hands and feet). In general terms it is usually well tolerated by patients.

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 (see below). The liver metabolizes it and side effects are similar to those of flecainide and are commoner 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.

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 heart potassium channels. 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 great caution and with periodic ECG monitoring.

Cautions: Sotalol by prolonging the recovery phase of the cardiac action potential can predispose to ventricular arrhythmias (torsade de pointes) that can be risky. To minimize the likelihood of this problem if there is evidence of renal impairment the dose needs review and reduction. In addition the potential risk of adverse reactions to sotalol increase if the potassium or magnesium concentrations in the blood are low.

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 with other effects including fatigue, sleep disturbance, shortness of breath, sexual dysfunction and depression.

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

Dronedarone

Dronedarone is a newly introduced drug that is similar to amiodarone in structure but has modifications to make its metabolism more clinically useful

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. It is the only anti-arrhythmic medication that has been demonstrated to improve outcome in AF in a large randomized clinical trial.

Contra-indications: Dronedarone is contraindicated in patients with severe heart failure (NYHA class IV or unstable class III), recent hospitalization with heart failure, or worsening heart failure symptoms. Dronedarone is also contraindicated in patients with severe hepatic or renal impairment. 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 torsade de pointes is very rare. Most side effects resolve within the first 2 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 also used when the heart has changed its rhythm (arrhythmia) to help it return to normal rhythm.

Side Effects

Although generally well tolerated amiodarone does have side effects that can affect different parts of our body.

Skin: When taking amiodarone the skin can take on a greyish/blue tinge. This will settle on stopping amiodarone.

While taking amiodarone you may become more sensitive to the harmful effects of sunlight. Using sunblock and hats appears to prevent this side effect. Because amiodarone remains in the body for a long time it may be necessary to continue using sunblock for a few months after stopping amiodarone.

Thyroid Gland: The thyroid gland produces a hormone which controls the body's metabolism. Amiodarone can affect this gland making it both over active (this occurs in about 2% of people taking amiodarone) or under active (this occurs in about 6% of people taking amiodarone). Your doctor will take regular blood tests to check if either of these has developed. If you experience symptoms of extreme tiredness or restlessness you should contact your general practitioner in normal surgery to discuss this. The doctor may wish for you to have a blood test if this has not been recently performed. Both an overactive and underactive thyroid can easily 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. You may however notice the effect of these eye deposits if looking at bright lights at night e.g. when driving a car. Of people taking amiodarone 1 in 10 will experience a bluish halo. Again this is not harmful.

Lungs: Amiodarone can cause problems with thickening (Fibrosis) of some of the structures of the lungs. If you feel you have problems with shortness of breath then you should arrange to see your general practitioner 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 affects listed above, although not common do mean that monitoring is important.

You will need to be reviewed by your general practitioner every six months whilst on amiodarone and they will need to arrange blood tests to ensure that your thyroid and liver function is acceptable and ensure that you are demonstrating no other problems.

Digoxin

Digoxin is a medication that has been used for many years. It was first described by a doctor called William Withering in 1785 when he found that the extracting the sap of the Foxglove could help patients suffering with 'Dropsy' (what we would now call heart failure).

As such it is often said to be the start of modern medicines. Opinion regarding the use of digoxin has been varied and this has continued to the present day.

Digoxin is a medication commonly used in the treatment of atrial fibrillation 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

It is usually prescribed as a once daily medication. However in most people you will find that the doctor asks you to initially take it twice daily to 'load' the body to make it more effective quicker.

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 (yellow-green halos around people or objects, some people describe these as auras), confusion, drowsiness, dizziness, nightmares, agitation.

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

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 to twice a year. Generally the affects of digoxin can be monitored just through the physical examination (taking the pulse and the blood pressure) but occasionally the doctor may ask for a blood test to be performed to check the level of the digoxin in the blood although this is not routine practice.

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. Please remember to always 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 investing in 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 – pharmacists occasionally make mistakes and sometimes your tablets may look different because they have come from a different manufacturer (even though the drug is the same).

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

Contact the 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 send advice to you about what to do. If you feel very unwell and are unable to contact your GP/doctor, you should consider attending the local Accident and Emergency Unit, taking all of your medication with you.

Some medication used to control AF stays in the body for quite a long time after stopping taking it and any side effects may take a while to diminish. Amiodarone (Cordarone X) is the most prominent drug that causes this problem; it takes many weeks to reach stable levels in the body and may take 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.

**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 doctor changes them or recommends another form of treatment.

Remember that new treatments for Atrial Fibrillation 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 or catheter ablation, possibly with an implant of 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.

Blood thinning medication

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 5 times greater than in the normal sinus rhythm (regular heart rhythm). This is why people with AF need to have their blood thinned to reduce the risk of clots forming and thus reduce the risk of strokes.

What blood thinning options are available for doctors to use?

Clots are made up of 2 main components from the blood. These two components are (i) fibrin, a long protein that binds together to form a mesh and (ii) platelets, small cell particles that stick to the mesh and help to hold it together once they become active. The blood can be thinned to different degrees by attacking each of these components. Drugs like warfarin and heparin act to stop the formation of fibrin and are known as anticoagulants, whilst aspirin and clopidogrel are drugs that stop the activation of platelets and are known as anti-platelet agents.

Anticoagulants

By inhibiting the formation of the fibrin network, warfarin and heparin act to thin the blood very efficiently and can reduce the risk of stroke by up to 60%.

Warfarin

At present only warfarin is available in tablet form and thus useful for long-term blood thinning. Warfarin acts on the liver to prevent the formation of the proteins that go on to create fibrin. As our bodies have stores of these proteins that last a few days warfarin will only start to thin the blood efficiently after a few days. In the same way when you stop warfarin it takes the body a couple of days to replace these proteins and so the blood thinning effect will remain for a few days after you stop. As well as acting on the liver, warfarin is removed from our bodies by the liver. We are all slightly different in how efficiently our liver removes warfarin as we are all slightly different in age, size and sex, and we all eat different foods, take different medications and drink different amounts of alcohol. This is why the dose of warfarin needs to be tailored to each individual and is also why the dose of warfarin needed can change from time to time, for instance drinking more alcohol when on holiday or taking a course of antibiotics for an infection. The effectiveness of warfarin is measured by the INR (international ratio) which compares how fast blood clots compared to an international standard. Normal blood clotting has an INR of 1.

To prevent the risk of stroke in AF the blood needs to be 2-3 times thinner, so that it takes two to three times longer to clot i.e. has an INR of 2-3. By measuring the INR, anticoagulant clinics ensure that your blood is thinned to just the right amount. Too little warfarin and you won't have the full benefit of preventing strokes, whereas too much warfarin (INR>3) thins the blood too much and can put you at risk of bleeding heavily when you cut yourself and of bruising badly when you fall.

When you first start taking warfarin you will attend the anticoagulant clinic weekly as they adjust your dose to suit you. Most people find once they are established on warfarin their INR is pretty stable and they need only attend the clinic every 6-8 weeks. However you have to watch out for things that can affect your warfarin level to keep it stable, such as alcohol, certain food items and other medication, including cough remedies, herbal cures and many other over-the-counter medications. In short you are fine to have a couple of paracetamol for a headache but anything else you should seek the advice of your doctor or chemist.

As your warfarin level can change without you realising it, you should take care to avoid cuts and bruises; for instance use a thimble if you are sewing, use an electric razor when shaving, although this can sound a bit daunting please remember that for the vast majority of people who taking warfarin there are few or no problems.

Heparin

At present heparin-based products can only be given by injection either into the skin or veins so are not useful for long-term blood thinning. Heparin thins the blood by blocking the proteins that form fibrin, and works quickly. Therefore heparins are very useful when the level of blood thinning needs to be changed quickly, for example some people when they first develop AF are at a high risk of strokes and so will be started on heparin to protect them immediately.

Anti-platelets

Aspirin and clopidogrel act in slightly different ways to prevent the activation of platelets. As they affect the platelets that are circulating in

the blood they are effective almost immediately. However as platelets are not so vital for clot formation in the atria they are less effective than anti-coagulants at preventing strokes reducing the stroke risk in AF by 20%. In some people who are at very low risk of stroke this is sufficient. There are no problems with dose changes with aspirin and clopidogrel so there is not the need to attend regular clinics and not the same worries about taking other medications or injury risks. Although both aspirin and clopidogrel do prolong bleeding and thus increase the risk of bruising this is much less than the risks with warfarin.

The main problem associated with anti-platelet medication is gastric ulcers and this is only a risk with aspirin, this risk can be significantly reduced by taking medications that reduce stomach acid which may be suggested by your doctor.

Which drug is best for me?

The choice of which drug is best for you depends on:- (i) your personal risk of stroke and (ii) if any intervention like cardioversion or ablation are planned.



Further information

For further information on Atrial Fibrillation, please contact the Atrial Fibrillation Association.

**Website: www.atrialfibrillation-au.org
www.afa-international.org**

Email: info@atrialfibrillation-au.org

Telephone: 1800 050 267 or (02) 61084602





Atrial Fibrillation Association

MEMBERSHIP APPLICATION

Register to become a member of AFA Australia on line at
www.atrialfibrillation-au.org
www.afa-international.org

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AFA Medical Advisory Committee:

Dr Michael Davis
Professor Ben Freedman
Dr Gerry Kaye

Director & Chief Executive:

Mrs Trudie Lobban

Assistant Director:

Mrs Jo Jerrome

Please remember these are general guidelines and individuals should always discuss their condition with their own doctor.



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