Amiodarone is used for the treatment of arrhythmias, particularly when other drugs are ineffective or contraindicated. Amiodarone should be initiated under hospital or specialist supervision.¹

**Note:** Amiodarone has been confused with other agents, notably allopurinol and amlodipine. Please take special care with these medicines when prescribing or dispensing.

**MAKE SURE THERE IS A PLAN FOR MONITORING AND DOSE ADJUSTMENT**

Although amiodarone is most frequently initiated in the hospital environment under specialist supervision,² long-term monitoring and evaluation often becomes the responsibility of the primary care team. Please ensure that there is clarity over who is ultimately responsible for organising, reviewing and acting upon monitoring information of amiodarone for each patient. Check that dose reductions occur post-discharge as planned. There have been cases of amiodarone toxicity when patients are discharged on their initial loading dose and this is continued at home. The high initial dose is necessary because amiodarone has a very long half-life and it takes time before the optimal tissue levels of amiodarone are achieved.³

**Recommended amiodarone dosing regime²**

<table>
<thead>
<tr>
<th>Week</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>200mg three times daily</td>
</tr>
<tr>
<td>Week 2</td>
<td>200mg twice daily</td>
</tr>
<tr>
<td>Week 3 onwards</td>
<td>200mg* daily</td>
</tr>
</tbody>
</table>

*or the minimum required to control the arrhythmia

It may take weeks or months to achieve steady-state plasma levels. Amiodarone may remain in the tissues for some time after the drug has been withdrawn. This is particularly important when monitoring for adverse effects because they may not become apparent until after amiodarone has stopped.¹

It is important that the minimum effective maintenance dose is used, especially in older adults³ who are more susceptible to bradycardia and conduction defects associated with higher doses. Further, thyroid function should also be closely monitored in older adults.³

**Note:** Some patients may have higher loading and maintenance doses of amiodarone under the direct supervision of a cardiologist.⁴

**CHECK LIVER FUNCTION AND THYROID FUNCTION EVERY 6 MONTHS**

**Liver function**

Amiodarone is associated with hepatotoxicity. Liver function tests are recommended at baseline and every 6 months during treatment. If serum transaminases are raised, a dose reduction is advisable. However if clinical signs of liver disease are evident, amiodarone should be stopped.¹² In rare circumstances, chronic liver disease can occur, including cirrhosis.²

**Thyroid function**

Amiodarone contains iodine and can cause disorders of thyroid function. Pre-existing thyroid dysfunction is a contraindication to amiodarone use.² Thyroid stimulating hormone (TSH) levels, and clinical symptoms of thyroid dysfunction (such as weight loss, angina and congestive heart failure) should be assessed before treatment, every 6 months during treatment, and for several months after discontinuation.³

**Note:** There may be a transient rise in TSH soon after initiating amiodarone due to the sudden iodine load, which can accelerate thyroid hormone synthesis. Levels should return to within the normal range after 3 months.⁵

*Note: some cardiologists recommend 3-monthly testing.

➥ continued
Hyperthyroidism is the most frequent adverse effect of amiodarone reported to CARM (Centre for Adverse Reaction Monitoring), with 47 cases reported in New Zealand during 2008-2013. Amiodarone-induced hyperthyroidism can develop rapidly and may present as a new arrhythmia. The occurrence, or recurrence of tachycardia or atrial fibrillation, is an indication to re-check thyroid function. Raised T3 and T4 levels with a very low or undetectable TSH concentration may suggest thyrotoxicosis. Amiodarone should be withdrawn temporarily to help achieve control. Treatment with carbimazole is usually required to block thyroid hormone synthesis while amiodarone is excreted. It may be possible to continue amiodarone under close supervision, with thyroxine replacement therapy added if necessary.

Hypothyroidism has also been associated with amiodarone use and does not appear to be dose-related. Patients should be informed about the symptoms of hypothyroidism (eg fatigue, cold intolerance and dry skin). If it is detected, refer to an endocrinologist for review. It may be possible to continue amiodarone under close supervision, with thyroxine replacement therapy added if necessary.

INVESTIGATE NON-PRODUCTIVE COUGH AND DYSPNOEA
Pulmonary toxicity (including pneumonitis and fibrosis) is the most serious and life-threatening adverse effect of amiodarone. It can develop rapidly; the incidence varies from 1-17%, with fatalities in approximately 10% of cases. Patients should be informed to report any non-productive cough or dyspnoea during amiodarone treatment because pneumonitis may be the cause. If suspected, stop amiodarone and arrange lung function tests and a chest X-ray. Fatalities usually arise following the progression of pulmonary fibrosis to respiratory failure. Some guidelines recommend annual chest X-rays; however the frequency may vary depending on individual patient risk factors. Although the risk of pulmonary adverse effects increases with cumulative high doses, they can also occur at low doses especially in elderly patients or those with pre-existing lung disease. Management usually involves a dose reduction or discontinuation depending on severity. Pulmonary adverse effects are usually reversible, although corticosteroid therapy may be required.

Cardiotoxicity is also a possibility with amiodarone treatment. The most serious effects, such as severe hypotension and sinus arrest, usually occur during intravenous infusion within the hospital setting. In primary care, excessive dosing may lead to bradycardia and conduction disturbances, especially in older patients, or when combined with other antiarrhythmic agents. If these effects occur, amiodarone should be temporarily withdrawn.

Pulmonary toxicity (including pneumonitis and fibrosis) is the most serious and life-threatening adverse effect of amiodarone. It can develop rapidly; the incidence varies from 1-17%, with fatalities in approximately 10% of cases.

Electrocardiogram (ECG) monitoring is recommended for patients on long-term therapy with amiodarone. Most guidelines advise annual ECG monitoring.

Note: Amiodarone can also cause hypokalaemia. If possible, avoid other agents that cause hypokalaemia such as stimulant laxatives and certain diuretics.

ADVISE PATIENTS ABOUT RISK OF PHOTOTOXICITY
Amiodarone causes photosensitivity reactions in many patients, which can lead to a wide variety of skin reactions. These range from an increased likelihood to suntan, to intense burning and swelling of exposed areas. Because of the possibility of phototoxicity, patients should be advised to protect their skin from natural and artificial sunlight during treatment and for several months after discontinuing amiodarone. A wide-spectrum sunscreen should be used to protect against both long-wave ultraviolet and visible light. A reduction in dosage may be required for some patients. A persistent slate-grey skin discolouration may occur in some patients. A dose reduction may help to avoid this pigmentation. Some patients may wish to discontinue amiodarone if it occurs and if other antiarrhythmic medicines are suitable, however discolouration can persist for up to 12 months after amiodarone has been stopped.
REFER TO AN OPHTHALMOLOGIST IF VISION BECOMES IMPAIRED

All patients experiencing new or worsening visual symptoms while taking amiodarone, should be referred for ophthalmological assessment.  

Most patients taking amiodarone develop corneal microdeposits; these are reversible on withdrawal, and sometimes following a reduction in dose. Although these deposits rarely interfere with vision, drivers may be dazzled by headlights at night.

More serious ocular effects include optic neuritis and optic neuropathy, which can progress to blindness. Optic neuropathy can present acutely or gradually, with decreased visual acuity, decreased colour vision, or visual field loss. Optic neuropathy usually occurs in both eyes within 12 months of starting amiodarone, and improves or resolves when it is discontinued. If vision is impaired, expert advice must be sought and amiodarone stopped.

Patients with pre-existing visual impairment should have an eye examination prior to amiodarone treatment. Enquire about possible ocular side effects at each visit, and arrange follow-up examinations for all patients who report visual symptoms.

Interactions with amiodarone

- there are a number of important interactions with amiodarone; some medicines are contraindicated in combination. The long half-life of amiodarone gives it the potential to cause interactions weeks after it has been withdrawn.
- clinically significant interactions of note involve digoxin and warfarin.
- amiodarone increases concentrations of digoxin; if both agents are absolutely necessary, a dose reduction of digoxin and careful monitoring are essential.
- amiodarone impairs the metabolism of warfarin, potentiating its anticoagulant effect and risk of bleeding. Dose reduction and weekly INR monitoring of warfarin are required until stable.

Please refer to:  
www.nzf.org.nz/stockleys/10758611000116106.html

for a comprehensive list.

RECOMMENDED AMIODARONE MONITORING

<table>
<thead>
<tr>
<th></th>
<th>BASELINE</th>
<th>FOLLOW UP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>6-monthly</td>
</tr>
<tr>
<td>Electrocardiogram (ECG)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Chest X-ray (CXR)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Thyroid function tests (TFTs)*</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Liver function tests (LFTs)*</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Pulmonary function tests (PFTs) Only if any symptoms of respiratory deficiency</td>
<td>Only for those with suspicious symptoms</td>
<td></td>
</tr>
<tr>
<td>Eye examination Only if pre-existing visual impairment</td>
<td>Slit lamp assessment suggested for those with suspicious symptoms</td>
<td></td>
</tr>
</tbody>
</table>

*Note: some cardiologists recommend 3-monthly testing.
REFERENCES


ACKNOWLEDGEMENTS

We wish to thank John Scott, Geriatrician and Clinical Director of Health of Elder Adults Services, and Chanelle Owen, Cardiology Pharmacist, Waitemata DHB, for their valuable contribution to this bulletin.