

## AMIODARONE - SAFE PRESCRIBING - KEEP AN EYE ON IT

1

- ▶ MAKE SURE THERE IS A PLAN FOR MONITORING AND DOSE ADJUSTMENT
- ▶ CHECK LIVER FUNCTION AND THYROID FUNCTION EVERY 6 MONTHS
- ▶ INVESTIGATE NON-PRODUCTIVE COUGH AND DYSPNOEA
- ▶ ADVISE ABOUT PHOTSENSITIVITY
- ▶ REFER TO AN OPHTHALMOLOGIST IF VISION BECOMES IMPAIRED

Amiodarone is used for the treatment of arrhythmias, particularly when other medicines are ineffective or contraindicated.<sup>1</sup> Amiodarone should be initiated under hospital or specialist supervision.<sup>2</sup>

**Note:** Amiodarone has been confused with other medicines such as allopurinol and amlodipine. Please take special care when prescribing, dispensing and administering these medicines.

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

Although amiodarone is most frequently initiated in the hospital environment under specialist supervision, 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 for everyone taking amiodarone.

Check that dose reductions occur post-discharge as planned. There have been cases of amiodarone toxicity when people are discharged with 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.<sup>3</sup>

#### Recommended amiodarone dosing regime<sup>4</sup>

Week	Dose
Week 1	200mg three times daily
Week 2	200mg twice daily
Week 3 onwards	200mg* daily

\*or the minimum required to control the arrhythmia

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

It can 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for some time after the drug has been withdrawn.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 still be apparent after amiodarone has stopped.<sup>2</sup>

It is important that the minimum effective maintenance dose is used, especially in older adults who are more susceptible to bradycardia and conduction defects with higher doses.<sup>3</sup> Thyroid function should also be closely monitored, particularly in older adults.<sup>3</sup>

In view of potential adverse effects associated with amiodarone, people who are particularly susceptible may be given amiodarone for a limited duration (eg 3 months). If this is the intention, the duration of treatment will be specified in the electronic discharge summary, and reviewed at the follow-up clinic appointment.

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

#### Liver function

Amiodarone is associated with dose-dependent hepatotoxicity. Liver function tests are recommended at baseline and every 6 months during treatment. If serum transaminases are raised, a dose reduction is advised; if clinical signs of liver disease are evident, amiodarone should be stopped.<sup>2,4</sup> In rare circumstances, chronic liver disease including cirrhosis can occur.<sup>4</sup> Due to the potential risk of hepatotoxicity and accumulation, amiodarone should be used with extreme caution if there is evidence of pre-existing hepatic disease.<sup>3</sup>

#### Thyroid function

Amiodarone contains iodine and can cause disorders of thyroid function. Pre-existing thyroid dysfunction or iodine hypersensitivity<sup>1</sup> is a contraindication to amiodarone use.<sup>4</sup> 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.<sup>3</sup>

→ continued

## AMIODARONE

2

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

**Hyperthyroidism** is a common adverse effect of amiodarone, it can develop rapidly and may present as a new arrhythmia.<sup>5</sup> The occurrence or recurrence of tachycardia or atrial fibrillation is an indication to re-check thyroid function.<sup>6</sup>

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, and treatment with carbimazole may be required.<sup>2</sup> Thyrotoxicosis can take several years to develop, and the classical signs such as goitre or ophthalmopathy may be absent.<sup>6</sup>

**Hypothyroidism** has also been associated with amiodarone use.<sup>6</sup> Patients should be informed about the symptoms of hypothyroidism (eg fatigue, cold intolerance and dry skin) and if it is detected, refer to an endocrinologist for review.<sup>6</sup> It may be possible to continue amiodarone under close supervision, with replacement therapy added if necessary.<sup>2</sup>

### INVESTIGATE NON-PRODUCTIVE COUGH AND DYSPNOEA

**Pulmonary toxicity** (including pneumonitis and fibrosis) can develop rapidly and can be a life-threatening adverse effect of amiodarone if diagnosis is delayed.<sup>7</sup>

People taking amiodarone should be informed to report any non-productive cough or dyspnoea during treatment because pneumonitis may be the cause.<sup>2</sup> If suspected, stop amiodarone, 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,<sup>8</sup> however the frequency may vary depending on individual risk factors.

Although the risk of pulmonary adverse effects increases with cumulative high doses, they can also occur at low doses especially in older adults and those with pre-existing lung disease.

Management usually involves a dose reduction or discontinuation depending on severity. Interstitial pneumonitis is generally reversible following early withdrawal of amiodarone, but in some cases corticosteroid therapy may be required.<sup>3</sup>

**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 adults or when combined with other antiarrhythmic medicines. If these effects occur, amiodarone should be temporarily withdrawn.<sup>3</sup>

Pro-arrhythmia (torsades) is rare when amiodarone is used alone but the risk increases when amiodarone is combined with other medicines that also prolong the QT interval (eg tricyclic antidepressants and sotalol). As with other antiarrhythmic medicines, it can be difficult to differentiate a lack of amiodarone efficacy from proarrhythmic effects.<sup>3</sup>

Electrocardiogram (ECG) monitoring is recommended for people receiving long-term therapy with amiodarone.<sup>3</sup> Guidelines generally advise annual ECG monitoring, or as clinically appropriate.<sup>1,9,10</sup>

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

### ADVISE ABOUT PHOTOSENSITIVITY

Amiodarone commonly causes photosensitivity, which can lead to a wide variety of skin reactions ranging from an increased likelihood of sunburn, to intense burning and swelling of exposed areas. Advise people to protect their skin from 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.<sup>2</sup> A dose reduction may be required for some people.<sup>3</sup>

A persistent slate-grey skin discolouration can also occur.<sup>4</sup> A dose reduction may help to reduce this pigmentation.<sup>3</sup> Some people may decide to discontinue amiodarone if other medicines are suitable, but the discolouration can persist for up to 12 months after amiodarone has been stopped.

### REFER TO AN OPHTHALMOLOGIST IF VISION BECOMES IMPAIRED

Everyone experiencing new or worsening visual symptoms while taking amiodarone should be referred for ophthalmological assessment.<sup>11</sup>

Many people taking amiodarone develop corneal micro-deposits which are reversible on withdrawal, and sometimes following dose reduction. These deposits rarely interfere with vision, but some 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

→ continued

## AMIODARONE

3

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.<sup>11</sup> If vision is impaired, expert advice must be sought and amiodarone stopped.<sup>2</sup>

If there is evidence of pre-existing visual impairment, an eye examination should be organised prior to amiodarone treatment. Enquire about possible ocular side effects at each visit and arrange follow-up examinations for anyone reporting visual symptoms.<sup>11</sup>

### INTERACTIONS WITH AMIODARONE

There are a number of important interactions with amiodarone, and some combinations are contraindicated. The long half-life of amiodarone gives it the potential to cause interactions for weeks after it has been withdrawn.<sup>8</sup> Clinically significant interactions of note:

**Digoxin** - amiodarone increases digoxin concentrations. If both are absolutely necessary, a dose reduction of digoxin and careful monitoring are essential.

**Warfarin** - amiodarone impairs the metabolism of warfarin, potentiating its anticoagulant effect and increasing the risk of bleeding. Dose reduction and weekly monitoring of warfarin are required until stable.<sup>8</sup>

Please refer to [www.nzf.org.nz](http://www.nzf.org.nz) for a comprehensive list

### Recommended amiodarone monitoring<sup>9</sup>

	Baseline	Follow up	
		6 monthly	Annually
Electrocardiogram (ECG)	✓		✓ *
Chest x-ray (CXR)	✓		✓
Thyroid function tests (TFTs)	✓	✓	
Liver function tests (LFTs)	✓	✓	
Pulmonary function tests (PFTs)	Only if symptoms of respiratory deficiency	Only if suspicious symptoms	
Eye examination	Only if visual impairment	Slit lamp assessment suggested if suspicious symptoms	

\*or as clinically appropriate

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For further information on other high-risk medicines visit our website at : [www.saferx.co.nz](http://www.saferx.co.nz)