SAFER
SAFER USE OF HIGH RISK MEDICINES

Waitemata District Health Board
Best Care for Everyone

AMIODARONE - SAFE PRESCRIBING - KEEP AN EYE ON IT

- 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 PHOTOSENSITIVITY
- REFER TO AN OPTHALMOLOGIST IF VISION BECOMES IMPAIRED

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

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 , long-term monitoring and evaluation often becomes the responsibility of the primary care team.

Check that dose reductions occur post-discharge as planned. 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.

Recommended amiodarone dosing regime

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

Amiodarone remains in the tissues for many months after being withdrawn. This is particularly important when monitoring for adverse effects because they can occur well after amiodarone has been stopped.

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.

Thyroid function

Amiodarone contains iodine and can cause disorders of thyroid function. Thyroid stimulating hormone (TSH) levels, and clinical symptoms of thyroid dysfunction should be assessed before treatment, every 6 months during treatment, and for several months after discontinuation.

Amiodarone-induced Hyperthyroidism can occur as long as a year after withdrawal of the medicine, depending on dose and duration of treatment.

Note: A transient rise in T4 can occur soon after initiating amiodarone due to an inhibition of T4 to T3 conversion but should return within range after 3-6 months.

Hyperthyroidism occurs in around 2 to 4% of amiodarone users. It can develop rapidly and may present as a new arrhythmia. Re-check thyroid function if tachycardia or atrial fibrillation occur. Thyrotoxicosis can take several years to develop, and the classical signs such as goitre or ophthalmopathy may be absent.

Raised T3 and T4 levels with a very low or undetectable TSH concentration suggest thyrotoxicosis. Stopping amiodarone will not hasten recovery as it stays in the body for a long time after cessation; discuss with the patient's cardiologist. Treatment with carbimazole and sometimes steroids may be required and the patient referred to an endocrinologist.

Hypothyroidism has also been associated with amiodarone use, more often in iodine replete areas. Patients should be informed about the symptoms such as fatigue, cold intolerance and dry skin, and if detected, referred to an endocrinologist for review. It may be possible to continue amiodarone under close supervision, with replacement therapy added if necessary

INVESTIGATE NON-PRODUCTIVE COUGH AND DYSPNOEA

Pulmonary toxicity including pneumonitis and fibrosis occurs in around 2%-5% of amiodarone recipients. It can

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develop rapidly and can be a life-threatening adverse effect of amiodarone if diagnosis is delayed. Patients should be informed to report any non-productive cough or dyspnoea. If pneumonitis is suspected, stop amiodarone, arrange lung function tests and a chest X-ray.

Although the risk of pulmonary adverse effects increases with cumulative high doses, they can 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.

Cardiotoxicity including severe hypotension and sinus arrest, can 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 with other antiarrhythmic medicines. If these effects occur, amiodarone should be temporarily withdrawn.

Pro-arrhythmia (torsades) is rare unless amiodarone is combined with other medicines that prolong the QT interval.

Electrocardiogram (ECG) monitoring is recommended for people receiving long-term therapy with amiodarone. Guidelines generally advise annual ECG monitoring, or as clinically appropriate.

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 increase the intensity of sunburn and cause swelling of exposed areas. Advise people to protect their skin from sunlight for several months after discontinuing amiodarone. A dose reduction may be required.

A persistent slate-grey skin discolouration can occur with long-term use. A dose reduction may help to reduce this but discolouration can persist for up to 12 months after amiodarone has been stopped.

REFER TO AN OPTHALMOLOGIST IF VISION BECOMES IMPAIRED

Everyone experiencing new or worsening visual symptoms while taking amiodarone should be referred for ophthalmological assessment. Corneal micro-deposits can occur; these are reversible on withdrawal, and sometimes following dose reduction. They rarely interfere with vision, but can dazzle drivers at night. More serious ocular effects include optic neuritis and optic neuropathy, which can progress to blindness.

Optic neuropathy can cause decreased visual acuity, decreased colour vision, or visual field loss. It usually occurs in both eyes within 12 months of starting amiodarone, and improves or resolves when discontinued. If there is evidence of pre-existing visual impairment, an eye examination should be organised prior to amiodarone treatment.

INTERACTIONS WITH AMIODARONE

There are a number of important interactions with amiodarone, and its long half-life can cause interactions for weeks after withdrawal. Amoidarone should generally be avoided with concurrent medicines that cause QT prolongation such as citalopram, erythromycin, ondansetron and digoxin.

Additional 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.

Dabigatran – The anticoagulant effect of dabigatran can be potentiated by the concurrent use of amiodarone, increasing the risk of bleeding.

Simvastatin and atorvastatin – the risk of myopathy may be increased; do not exceed 20mg per day of simvastatin if taking amiodarone

Please refer to www.nzf.org.nz for a comprehensive list

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Recommended amiodarone monitoring

	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

REFERENCES

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2. Sanofi-Aventis New Zealand Limited. Cordarone X Data Sheet. 20-09-16 www.medsafe.govt.nz/profs/datasheet/c/CordaroneXtabinj.pdf (Accessed 08-02-19)
3. Amiodarone, New Zealand Formulary www.nzf.org.nz/nzf_1090.html?searchterm=amiodarone (Accessed 08-02-19)

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CLICK HERE FOR FURTHER INFORMATION ON AMIODARONE AND A FULL REFERENCE LIST

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