PrescQIPP Community Interest Company

Dronedarone and amiodarone prescribing

In England and Wales £8.9 million is spent annually on antiarrhythmic drugs, of which £1.5 million is for dronedarone and £1.4 million is on amiodarone (NHSBSA October 2018 to September 2019).

QIPP projects in this area are aimed at reviewing the continued need for dronedarone and amiodarone and switching to an alternative product with better safety and efficacy and a lower acquisition cost. This bulletin reviews the place in therapy of dronedarone and amiodarone and offers guidance and support material for organisations considering reviewing their prescribing as a QIPP project. This bulletin only considers use in adults, paediatric patients (including those requiring an unlicensed liquid preparation) must be referred to a consultant cardiologist for advice on appropriate therapy.

Recommendations

- Ensure that prescribing of dronedarone and amiodarone is in line with NICE guidance for the management of atrial fibrillation (Clinical Guideline 180).
- Ensure that prescribing of dronedarone is in line with NICE guidance for the treatment of non-permanent atrial fibrillation (Technology Appraisal 197).
- Commence new patients with atrial fibrillation on a treatment recommended by NICE.
- Amiodarone or dronedarone should not be initiated in primary care. They must be initiated by a specialist and only be continued under a shared care arrangement for patients where other treatments cannot be used.
- Review all patients on dronedarone or amiodarone for suitability for switching to an alternative product. Switch all suitable patients to an appropriate treatment option.
- As with all switches, these should be tailored to the individual patient.

National Guidance

NICE Clinical Guideline 180 covers the management of atrial fibrillation in adults and recommends rate control as the first-line strategy for people with atrial fibrillation, except in certain circumstances.[1]

For most people with atrial fibrillation who need drug treatment as part of a rate control strategy, a standard beta-blocker (that is, a beta-blocker other than sotalol) or a rate-limiting calcium-channel blocker will be appropriate as initial monotherapy.[1]

If monotherapy does not control symptoms resulting from poor ventricular rate control, the addition of diltiazem or digoxin are appropriate for combination therapy.[1] Amiodarone should not be used for long-term rate control.[1]

Rhythm control may be considered when symptoms continue after heart rate has been controlled or for whom a rate-control strategy has not been successful.[1] Where cardioversion is suitable, amiodarone may be used for 4 weeks before and 12 months after cardioversion.[1]

Amiodarone should also be considered for people with left ventricular impairment or heart failure, for people with atrial fibrillation whose symptoms continue after heart rate has been controlled or for whom a rate-control strategy has not been successful.[1] It may be used as pharmacological cardioversion in new onset atrial fibrillation in people with evidence of structural heart disease and also in people undergoing cardiothoracic surgery to reduce the risk of post-operative atrial fibrillation.[1]

If drug treatment is needed for long-term rhythm control, a beta blocker (other than sotalol) should be used as first-line treatment unless there are contraindications.[1] If beta blockers are contraindicated or unsuccessful the patient may be suitable for dronedarone or amiodarone in the specific circumstances outlined.

Dronedarone can be used as an option for the maintenance of sinus rhythm after successful cardioversion in people with paroxysmal or persistent atrial fibrillation whose atrial fibrillation is not controlled by first line therapies and after alternative options have been considered and who have at least one of the cardiovascular risk factors outlined by NICE.[1,2]

NHS England has reviewed this information and determined that dronedarone and amiodarone are products that should not be routinely prescribed in primary care based on the risk of potentially fatal long-term side-effects and alternative treatments being available for use in atrial fibrillation.[3]

Clinical Effectiveness

A rate control strategy is more important than a rhythm control strategy because it is effective for the majority of patients with atrial fibrillation, uses less toxic drugs and reduces the risk of harm.[4] However, in a smaller minority of patients rhythm control may be preferred.[4] Overall, until rhythm control strategies are more effective, rate control is the most important initial objective for most people with atrial fibrillation.[4]

Safety

Amiodarone can cause serious adverse reactions affecting the eyes, heart, lung, liver, thyroid gland, skin and peripheral nervous system.[5] When dronedarone came to the market, it was initially thought to be a safer option. However, a Europe-wide review was established to investigate concerns over post marketing reports of liver injury.[6] In addition, the 2011 PALLAS study (Permanent Atrial fibriLLAtion outcome Study using dronedarone on top of standard therapy), which was set up to investigate some of the potential clinical benefits of dronedarone, had to be terminated early when an interim analysis showed significantly more cardiovascular (CV) related deaths, stroke, and hospitalisations due to CV events in the dronedarone group compared with placebo.[6]

A combined review of these adverse outcomes by the EU Committee for Medicinal Products for Human Use (CHMP) considered that the benefits of treatment now continue to outweigh the risks only in a restricted patient population.[6] Consequently, in light of safety concerns, dronedarone should only be prescribed after other safer treatment options have been considered.[6]

Patient factors

There are alternative preparations available for the treatment of atrial fibrillation for the majority of patients, so no significant patient factors are foreseen. For those patients who fall into the restricted population where dronedarone or amiodarone is appropriate, then treatment may continue with appropriate monitoring.

Costs

There is a significant difference in cost between different pharmacological treatments for atrial fibrillation. Table 1 below illustrates the cost differences.

Table 1: Atrial fibrillation product and price comparison – Drug Tariff November 2019.[7]

Product*	Cost per 28 days
Atenolol 25 mg tablets	£0.72
Bisoprolol 2.5 mg tablets	£0.85
Diltiazem 120 mg MR capsules (as Adizem-XL)	£9.14
Digoxin 125 mcg tablets	£1.61
Amiodarone 200 mg tablets	£2.82
Dronedarone 400 mg tablets	£63.00

*Preparations included in this table provide an example of commonly prescribed strengths only and should not be taken to imply equivalence.

Switching options

There are several potential options for switching from dronedarone and amiodarone to alternatives which are dependent on other treatments for atrial fibrillation already prescribed or considered (although clinicians may choose other options according to the clinical need of the patient). These include:

1. If monotherapy with a rate control drug OR long-term rhythm control is indicated, a low cost standard beta blocker (atenolol or bisoprolol) is preferred.
2. If combination therapy is indicated for rate control, the addition of once daily modified-release diltiazem or digoxin should be considered second-line. Note, diltiazem is unlicensed for this indication.

Switch Savings

There is a significant difference in cost between dronedarone or amiodarone and alternative rate or rhythm control treatments for atrial fibrillation. In England and Wales, around £1.5 million is spent on dronedarone per year and around £1.4 million is spent on amiodarone per year. Switching from dronedarone or amiodarone to an alternative product could release savings of up to £2.14 million nationally. This equates to savings of £3,828 per 100,000 patients.

Summary

Where pharmacological treatment of atrial fibrillation is indicated, rate control is effective for most patients, uses less toxic drugs and reduces the risk of harm. For the smaller proportion of patients who require rhythm control, dronedarone and amiodarone should only be used in the specific circumstances for which they are indicated, due to the safety risks associated with these drugs. Other safer treatment options should be tried first, wherever possible. Consequently, dronedarone and amiodarone are not recommended for routine prescribing in primary care.

References

1. National Institute for Health and Care Excellence (NICE). Clinical Guideline 180. Atrial Fibrillation: management. Published June 2014, last updated August 2014. Available at: https://www.nice.org.uk/guidance/cg180 Last accessed 18/09/19.
2. National Institute for Health and Care Excellence (NICE). Technology Appraisal 197. Dronedarone for the treatment of non-permanent atrial fibrillation. Published August 2010, last updated December 2012. Available at: https://www.nice.org.uk/guidance/ta197 Last accessed 18/09/19.
3. NHS England. Items which should not routinely be prescribed in primary care: Guidance for CCGs. Version 2. June 2019. Available at: https://www.england.nhs.uk/medicines/items-which-should-not-be-routinely-prescribed/ Last accessed 01/11/19.

4. Betts T, Mitchell A. Head to head: Is rate more important than rhythm in treating atrial fibrillation? BMJ 2009;339: b3173. Available at: https://www.bmj.com/bmj/section-pdf/186337?path=/bmj/339/7722/Head_to_Head.full.pdf Last accessed 18/09/19.
5. Electronic Medicines Compendium (eMC). Summary of Product Characteristics (SPC) for amiodarone 200 mg tablets. Accord Healthcare Limited. May 2017. Available at: https://www.medicines.org.uk/emc/product/6018/smpc Last accessed 18/09/19.
6. Medicines & Healthcare products Regulatory Agency. Dronedarone (Multaq): cardiovascular, hepatic and pulmonary adverse events - new restrictions and monitoring requirements. Drug Safety Update Oct 2011, vol 5 issue 3: A1. Available at: https://www.gov.uk/drug-safety-update/dronedarone-multaq-cardiovascular-hepatic-and-pulmonary-adverse-events-new-restrictions-and-monitoring-requirements Last accessed 18/09/19.
7. National Health Service Business Services Authority. Department of Health. Drug Tariff. November 2019. Available at https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/drug-tariff Last accessed 01/11/19.

Implementation tools	https://www.prescqipp.info/our-resources/bulletins/bulletin-248-amiodarone-and-dronedarone/
Data pack	https://pdata.uk/#/views/B248_NHSELPP-Dronedaroneanda-miodarone/FrontPage?:iid=1

Information compiled by Gemma Dowell, PrescQIPP CIC, December 2019 and reviewed by Katie Smith, PrescQIPP CIC February 2020. Non-subscriber publication April 2021.

Contact help@prescqipp.info with any queries or comments related to the content of this document.

This document represents the view of PrescQIPP CIC at the time of publication, which was arrived at after careful consideration of the referenced evidence, and in accordance with PrescQIPP's quality assurance framework.

The use and application of this guidance does not override the individual responsibility of health and social care professionals to make decisions appropriate to local need and the circumstances of individual patients (in consultation with the patient and/or guardian or carer). Terms and conditions