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Position Statement for the Prescribing of Dronedarone In Atrial Fibrillation

South West London CCGs* (in line with NHS England's national guidance on medicines which should no longer be routinely prescribed) **do not support the routine prescribing of dronedarone for the treatment of atrial fibrillation (AF).**[1]

Dronedarone should only be initiated under hospital or specialist supervision and no new patients should be initiated on dronedarone in primary care.

Rationale

NICE guidance (updated Dec 2012): Dronedarone therapy may be considered for the maintenance of sinus rhythm after successful cardioversion in clinically stable patients with paroxysmal or persistent AF, and who are not controlled by first line treatments (usually including beta-blockers) in patients:

- who have at least 1 of the following cardiovascular (CV) risk factors: hypertension requiring drugs of at least 2 different classes, diabetes mellitus, previous transient ischaemic attack, stroke or systemic embolism, left atrial diameter of 50 mm or greater, or age 70 years or older, and
- who do not have left ventricular systolic dysfunction nor a history of, or current, heart failure.[2]

This follows data from the PALLAS study (Permanent Atrial fibrillation outcome Study using dronedarone on top of standard therapy) in patients older than 65 with permanent atrial fibrillation. The study was prematurely terminated in July 2011, when an interim analysis showed a significant excess of cardiovascular -related deaths, stroke, and hospitalisations due to CV events in the dronedarone group compared with placebo.[3]

The EU Committee for Medicinal Products for Human Use (CHMP) reviewed risks and benefits of treatment with dronedarone after reports of liver injury, including two cases of liver failure requiring transplantation. The review was extended to include CV and pulmonary safety after the premature termination of PALLAS and several reported cases of pulmonary injury.[4]

References:

1. NHS England. Items which should not routinely be prescribed in primary care: Guidance for CCGs. https://www.england.nhs.uk/publication/items-which-should-not-be-routinely-prescribed-in-primary-care-guidance-for-ccgs/ (updated August 2019)
2. NICE guidance: www.nice.org.uk/guidance/ta197: Dronedarone for the treatment of non-permanent atrial fibrillation (updated December 2012**)**
3. https://www.nejm.org/doi/full/10.1056/nejmoa1109867 Dronedarone in high-risk permanent atrial fibrillation; Connolly S et al; N Engl J Med 2011; 365:2268-2276.
4. MHRA: Dronedarone (Multaq▼): cardiovascular, hepatic and pulmonary adverse events – new restrictions and monitoring requirements https://www.gov.uk/drug-safety-update/dronedarone-multaq-cardiovascular-hepatic-and-pulmonary-adverse-events-new-restrictions-and-monitoring-requirements
5. British National Formulary: https://bnf.nice.org.uk/medicinal-forms/dronedarone.html
6. Summary of product characteristics for dronedarone: https://www.medicines.org.uk/emc/medicine/22894/SPC/Multaq+400mg+tablets/

On-line references accessed 20/11/19

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Guidance for clinicians:

Please follow MHRA Advice for healthcare professionals[4] (see below)

Dronedarone is now contra-indicated in patients with:

- unstable haemodynamic conditions
- history of, or current, heart failure or left ventricular systolic dysfunction
- permanent AF (i.e. duration ≥6 months or unknown, and attempts to restore sinus rhythm no longer considered by physician)
- liver and lung toxicity related to previous use of amiodarone

Review patients prescribed dronedarone alongside cardiology expertise to determine the risk: benefit of continued therapy.

For patients continuing on dronedarone therapy please monitor:

1) **Cardiovascular:**

- Patients should receive regular cardiac examinations, including an electrocardiogram (ECG) at least every 6 months, to identify those who revert to AF. Discontinuation of dronedarone should be considered for these patients.
- Discontinue treatment if the patient develops permanent AF.
- Patients should be carefully evaluated for symptoms of heart failure during treatment.
- Patients should be appropriately anticoagulated as per local AF guidance, and in patients taking warfarin, the international normalisation ratio (INR) should be carefully monitored as dronedarone can affect INR.

2) **Hepatic:**

- Liver-function tests should be checked before starting treatment with dronedarone, after 1 week of treatment, after 1 month of treatment, then every month for 6 months, at month 9, at month 12, and periodically thereafter (at least annually and as clinically indicated).

3) Renal:

- Plasma creatinine values should be measured before and 7 days after initiation of dronedarone, and renal function should be monitored periodically afterwards.
- Discontinue treatment in any patients with further elevations of serum creatinine.

4) Pulmonary:

- Cases of interstitial lung disease, including pneumonitis and pulmonary fibrosis, have been reported in association with dronedarone. Onset of dyspnoea or non-productive cough may be related to pulmonary toxicity. If pulmonary toxicity is suspected during treatment, relevant lung examinations should be considered and treatment discontinued if confirmed.

Advice for patients:

Do not stop taking dronedarone unless your doctor has advised you to considering the risks and benefits of treatment.

Discuss your treatment with your hospital doctor and/or cardiologist at your next routine appointment.

A patient information leaflet is also available: https://www.prescqipp.info/items-which-should-not-routinely-be-prescribed-patient-leaflets

The NHS belongs to YOU, use it responsibly

*SWL CCGs (NHS Croydon CCG, NHS Kingston CCG, NHS Merton CCG, NHS Richmond CCG, NHS Sutton CCG and NHS Wandsworth CCG) position statement on dronedarone