South East London Area Prescribing Committee
Position Statement

Reference:	**PS-024**
Intervention:	**Dronedarone for the maintenance of sinus rhythm after successful cardioversion in patients with non-permanent (paroxysmal/persistent) atrial fibrillation (AF)**
Date of Decision:	**February 2020**
Date of Issue:	**March 2020**
Recommendation:	**RED – Suitable for prescribing and supply by hospital only** **Dronedarone should only be initiated under hospital or specialist supervision and no new patients should be initiated on dronedarone in primary care.**
Further Information:	• **Dronedarone is included in updated guidance from NHS England on low priority products as a medicine less suitable for routine prescribing in primary care [1].** • The NICE clinical guideline on AF CG 180 puts greater emphasis on rate rather than rhythm control and has clarified the place of dronedarone in the treatment pathway. • NICE technology appraisal guidance (updated Dec 2012) states: 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 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.[1] 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 CV-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] **For patients who remain on dronedarone, the MHRA advice for healthcare professionals[4] should be followed:** 1. Dronedarone is now contraindicated 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 2. Cardiovascular monitoring: • Patients should receive regular cardiac examinations, including an 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.

Further Information (cont'd):	3. Hepatic monitoring: • Liver-function tests should be done 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. 4. Renal monitoring: • 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. 5. Pulmonary monitoring: • 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 healthcare professionals, patients and carers:** • Patients should be advised to make a routine appointment to discuss their treatment with the treating physician, but should not stop taking dronedarone unless told to do so. • Review patients prescribed dronedarone with cardiology expertise to determine the risk: benefit of continued therapy.Patients currently prescribed dronedarone should be reviewed with input from their cardiologist (e.g. *advice and guidance/e-consult*) and/or ensure dronedarone is discussed at the patient's next routine cardiology appointment. • Patients who do not meet the above criteria who are currently receiving dronedarone should have the option to continue treatment until they and their clinician consider it appropriate to stop.
Cost impact for agreed patient group	There is a low spend on dronedarone in primary care across SEL (<£20K). Review of prescribing is likely to reduce this spend, whilst improving patient safety.
Usage Monitoring & Impact Assessment	**Acute Trusts** • Monitor use and audit use upon request to ensure use is in line with this position statement.
	CCGs • Monitor Epact 2 data, review of prescribing data in 6 months' time. • Monitor exception reports from GPs if inappropriate transfer of prescribing to primary care is requested.
Evidence reviewed:	1. NHS England and NHS Improvement: Items which should not be routinely prescribed in primary care: advice for CCGs, June 2019 https://www.england.nhs.uk/wp-content/uploads/2019/08/items-which-should-not-routinely-be-prescribed-in-primary-care-v2.1.pdf 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*

NOTES:

a) Area Prescribing Committee recommendations, position statements and minutes are available publicly via the APC website.

b) This Area Prescribing Committee position statement has been made on the cost effectiveness, patient outcome and safety data available at the time. The position statement will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued

c) Not to be used for commercial or marketing purposes. Strictly for use within the NHS.