NHS England Guidance: Medicines of Low Value

DRONEDARONE POSITION STATEMENT

Summary

The routine initiation of dronedarone is not recommended by NHS WEL CCGs. This is in line with NHS England's national guidance on items which should not routinely be prescribed (1).

Dronedarone is **Amber (Specialist initiated – Primary Care to continue)** for those patients who meet the exceptionality criteria.

- **New Patients:** Primary care Prescribers should not initiate dronedarone for any new patient unless they meet the exceptions criteria (1).
- **Existing patients:** All patients established on dronedarone should be reviewed for suitability of therapy. Ensure there is a clear indication for dronedarone therapy and this is documented in the patient record. If patients are found to revert back to atrial fibrillation, in agreement with a Specialist, switch to an appropriate treatment option.

- **Exceptions:** must be initiated by a Specialist and only continued* for patients where other treatments cannot be used, have failed or is in line with NICE Guidance NG196.

NHS England category: Products of low clinical effectiveness, where there is a lack of robust evidence of clinical effectiveness or there are significant safety concerns (1).

***Disclaimer**: NHSE recommend that dronedarone should only be continued under a under a shared care arrangement. Historically in WEL CCGs, dronedarone has held amber status on the formulary (Specialist Initiated – Primary Care to continue). In consultation with Cardiology colleagues at Barts Health NHS Trust, it has been agreed at the Waltham Forest & East London Medicines Optimisation and Commissioning Committee to maintain this formulary status locally in WEL CCGs, with the development of Primary Care prescriber information to support safe prescribing and management in Primary Care (see Appendix I).

Dronedarone is an analogue of the antiarrhythmic amiodarone. Following a review of its originally licensed indication, dronedarone is now used for the maintenance of sinus heart rhythm after cardioversion in clinically stable patients with paroxysmal or persistent atrial fibrillation, when alternative treatments are unsuitable (initiated under specialist supervision) (1,2).

NICE guideline on Atrial Fibrillation (AF) NG 196 puts greater emphasis on rate rather than rhythm control and has clarified the place of dronedarone in the treatment pathway (1).

Careful monitoring of dronedarone is essential and requires regular monitoring and caution due to the number of potential drug interactions (2); Primary Care prescriber information (see Appendix I) help clarify the responsibilities of primary care.

Advice for Primary Care

1. Ensure there is a clear indication for dronedarone therapy and this is documented in the patient record.
2. Review all patients on dronedarone and assess the suitability of switching to an alternative if they are in atrial fibrillation.
3. In agreement with Specialists in Secondary Care, de-prescribe dronedarone if not indicated. Switch all suitable patients to an appropriate treatment option.
4. If on-going treatment with dronedarone is indicated:
    - Prescribe in-line with the national recommendations (new patients)
    - Monitor the patient as set out in appendix 1. In summary after initiation this should be a minimum of every six months. Note that after initiation monthly LFT monitoring is required for the first 6 months, then at month 9 and 12, then 6 monthly thereafter.
    - Check for adverse effects and signs of toxicity
    - Check the dronedarone dosage
    - Check for drug interactions

    Refer also to Primary Care Prescriber information (see Appendix I).

Resources

PrescQIPP on behalf of NHS England have developed a Patient Information Leaflet (available here).

References

1. **NHS England and NHS Clinical Commissioners.** *Items which should not routinely be prescribed in primary care: Guidance for CCGs:* NHS England, [Online] June 2019 https://www.england.nhs.uk/medicines/items-which-should-not-be-routinely-prescribed/
2. **Optum in partnership with The Centre for Medicines Optimisation at Keele University**. *ScriptSwitch Rapid Update:* New Products added to NHS England's List of 'low priority' treatments. 1 July 2019

Acknowledgements

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Appendix 1: Primary Care Prescriber Information - Dronedarone

Dronedarone is an analogue of the antiarrhythmic amiodarone. Following a review of its originally licensed indication, dronedarone is now used for the maintenance of sinus heart rhythm after cardioversion in clinically stable patients with paroxysmal or persistent atrial fibrillation, when alternative treatments are unsuitable (initiated under specialist supervision).

The routine initiation of dronedarone is not recommended by NHS WEL CCGs. This is in line with NHS England's (NHSE) national guidance on items which should not routinely be prescribed. Dronedarone is Amber (Specialist initiated – Primary Care to continue) for those patients who meet the exceptionality criteria as outlined in the indication box below.

NHSE recommend that dronedarone should only be continued under a under a shared care arrangement. Historically in WEL CCGs, dronedarone has held amber status on the formulary (Specialist Initiated – Primary Care to continue). In consultation with Cardiology colleagues at Barts Health NHS Trust, it has been agreed at the Waltham Forest & East London Medicines Optimisation and Commissioning Committee to maintain this formulary status locally in WEL CCGs. This Primary Care prescriber information has been developed to support the safe prescribing and management of dronedarone in Primary Care.

For further information on the properties of dronedarone, please refer to the current Summary of Product Characteristics (www.medicines.org.uk) and BNF monograph

Indication	**Route & Dose**	**Contraindications to dronedarone administration**	**Actions and Monitoring undertaken by specialist before initiation**	**Duration of treatment**	**Stopping criteria**	**Follow up and on-going monitoring by the GP**
Maintenance of sinus rhythm after cardioversion in clinically stable patients with paroxysmal or persistent atrial fibrillation, when alternative treatments are unsuitable (initiated under specialist supervision), or is in line with NICE Guidance 196. Dronedarone should only be initiated in hospital or under	Oral: 400mg twice daily	• Hypersensitivity to the active substance or to any of the excipients listed in the SPC. • Second or third degree atrioventricular block, complete bundle branch block, distal block, sinus node dysfunction, atrial conduction defects, or sick sinus syndrome (except when used in conjunction with a functioning pacemaker) • Bradycardia <50 beats per minute (bpm) • Permanent AF with an AF duration ≥6 months (or duration unknown) and attempts to restore sinus rhythm no longer considered by the physician	• ECG: Ensure patient remains in sinus rhythm and that heart rate >50bpm • U&E's: An increase in plasma creatinine (10micromol/L) is expected	Long term	Patients reverting to atrial fibrillation will need review by specialist Pulmonary toxicity (rare cases of post marketing observation of interstitial lung disease) – onset of dsypnoea or	See table below.

specialist supervision in an out-patient setting.		• Patients in unstable hemodynamic conditions • History of, or current heart failure or left ventricular systolic dysfunction • Patients with liver and lung toxicity related to the previous use of amiodarone • Co-administration with potent cytochrome P 450 (CYP) 3A4 inhibitors • Medicinal products inducing torsades de pointes such as phenothiazines, cisapride, bepridil, tricyclic antidepressants, terfenadine and certain oral macrolides (such as erythromycin), Class I and III antiarrhythmics • QTc Bazett interval ≥500 milliseconds • Severe hepatic impairment • Severe renal impairment (CrCl <30 ml/min) • Pregnancy • Lactation	on initiation and plateaus after 7 days. If further increases are noted then discontinue treatment • Liver function: See table below. If ALT>3x upper limit of normal (ULN), withhold and re-measure within 48 hours. If remains 3xULN then withdraw treatment		non-productive cough treatment withheld – if pulmonary toxicity confirmed to discontinue treatement. If ALT>3x upper limit of normal (ULN), withhold and re-measure within 48 hours. If remains 3xULN then withdraw treatment See table below	
Key Safety Notices (for instance: notification if prescribing must be brand specific or BNF cautionary and advisory warnings): **-**						

Dronedarone Monitoring Requirements

Summary of dronedarone monitoring[1] - *for full detail please refer to the SPC*						
What to monitor:		**Rationale (% risk per annum)**	**Baseline**	**7 days**	**Every month for 6 months**	**After 6 months:**
ECG (SR / AF / other)		Check ECG abnormalities and ensure patient remains in SR Note bradycardia can occur in 1-10%	✓			Every 6 months
U&Es	Potassium	Deficiencies in electrolytes may precipitate arrhythmias.	✓			
	Magnesium		✓			
	Creatinine	Blood creatinine increase (>10%)	✓	✓	If clinically indicated	
Liver function	ALT	Liver function test abnormalities 1-10%. Hepatocellular liver injury, including life-threatening acute liver failure (0.1 to 0.01%)	✓	✓	✓	At month 9 and 12 then every 6months
Check for drug interactions		Dronedarone is primarily metabolised by CYP 3A4 inhibitors and inducers of CYP 3A4 have the potential to interact on dronedarone. Check SPC or BNF for full details **Clinically important interactions** (please note this is not a complete list – please refer to the current BNF or SPC for further information): • **Grapefruit juice -** Patients should be advised to avoid grapefruit juice while taking dronedarone due to inhibition of the CYP 3A4 enzymes leading to elevated levels. • **Statins -** there have been reported cases of rhabdomyolysis when dronedarone was given in combination with statins (simvastatin in particular). It is recommended that concomitant use of statins should be undertaken with caution and that lower starting doses and maintenance doses of statins should be considered according to the statin label recommendations. • **Digoxin** - if used concomitantly the dose of digoxin should be reduced by approximately 50% and serum levels of digoxin should be closely monitored with clinical and ECG monitoring. • **Warfarin -** INR levels can be affected by dronedarone therefore regular monitoring of warfarin is required when starting therapy. • **Dabigatran** - should not be used with dronedarone.				
Misc		Cases of interstitial lung disease including pneumonitis and pulmonary fibrosis have been reported in post- marketing experience. Onset of dyspnoea or non-productive cough may be related to pulmonary toxicity and patients should be carefully evaluated clinically. If pulmonary toxicity is confirmed treatment should be discontinued.				

[1] Summary of Product Characteristics, Dronedarone 400mg film-coated tablets (Multaq), Sanofi https://www.medicines.org.uk/emc/product/497/smpc last updated 02/06/2020, accessed 19/05/2021

Document Management

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