NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Consideration of consultation responses on review proposal

Review of TA197; Dronedarone for the treatment of non-permanent atrial fibrillation

This guidance was issued August 2012 with a review date of March 2013

Background

At the GE meeting of 26 June 2012 it was agreed we would consult on the review plans for this guidance. A four week consultation has been conducted with consultees and commentators and the responses are presented below.

Proposal put to consultees:	The guidance should be incorporated into the ongoing update of NICE clinical guideline 36 'Atrial fibrillation', once the wording of the guidance has been amended to reflect the changes to the UK marketing authorisation for dronedarone. That we consult on this proposal.
Rationale for selecting this proposal	Following safety concerns, the European Medicines Agency has reviewed and amended the marketing authorisation for dronedarone. This has resulted in a more restricted marketing authorisation than was originally appraised in TA197. However, the evidence suggests that reviewing the guidance would not be of value to the NHS. There is no new evidence to indicate that dronedarone would be less safe or less effective in the population that meets the revised marketing authorisation. Consequently, if considered in line with the revised marketing authorisation, it is likely that dronedarone would still be considered clinically and cost effective and continue to be recommended for this population. Therefore, it is proposed that the wording of recommendation 1.1 in TA197 is amended to reflect the changes in the UK marketing authorisation and the guidance re-issued accordingly.

	The Centre for Clinical Practice is currently updating NICE clinical guideline 36 'Atrial Fibrillation' and it is recommended that TA197 be incorporated into the update of CG36, once the wording of recommendation 1.1 has been amended to reflect the revised marketing authorisation. Any change in the treatment pathway, and therefore the relevant comparators for dronedarone would be identified during the guideline update. In the meantime, a warning about the restricted use of dronedarone should be placed on TA197 webpage of the NICE website.

GE is asked to consider the original proposal in the light of the comments received from consultees and commentators, together with any responses from the appraisal team. It is asked to agree on the final course of action for the review.

Recommendation post consultation:	The guidance should be incorporated into the ongoing update of NICE clinical guideline 36 'Atrial fibrillation', once the wording of the guidance has been amended to reflect the changes to the UK marketing authorisation for dronedarone.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
The Heart Failure Research Group		This document was a bit hard to follow but if you mean you plan to recommend restricting dronedarone as shown in the table on page 5 (pasted below), then I think that is certainly an improvement. However, you must recognise that the distinction between persistent and permanent AF is difficult and artificial – a patient can, literally, one day have persistent AF (and a possible indication for dronedarone) and permanent the	Thank you for your comment. NICE issues its guidance within the scope of the UK marketing authorisation. With this in mind, it should be noted that section 4.1 of the Summary of Product Characteristics for dronedarone states: "MULTAQ is indicated for the maintenance of sinus rhythm after successful cardioversion in

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		next (and a contraindication to dronedarone). Maybe one thing you should think of is what to advise if a patient DOES develop recurrence of AF after cardioversion – should you clearly state that dronedarone is stopped? Patients with AF also develop heart failure and left ventricular systolic dysfunction and consequently, if on dronedarone, should have it stopped. Which of course assumes they are being followed by a physician alert to these issues. I'm sure you can sense that I'm questioning whether there really is any role for dronedarone in routine clinical practice (especially as it has been shown to be less effective than an alternative, amiodarone, which can be used in patients with heart failure etc).	adult clinically stable patients with paroxysmal or persistent atrial fibrillation (AF). Due to its safety profile (see sections 4.3 and 4.4), Multaq should only be prescribed after alternative treatment options have been considered. MULTAQ should not be given to patients with left ventricular systolic dysfunction or to patients with current or previous episodes of heart failure". This makes it clear that dronedarone would not normally be a first-choice treatment and that there are safety concerns associated with this drug. The proposed wording for the revised recommendation states that dronedarone "is an option" for patients with AF that meet the specified criteria, thereby allowing prescribers to exercise their clinical judgment about which treatment would be the most appropriate.
Healthcare Improvement Scotland	No Comments	No comments to make	Comment noted. No changes required.
Royal College of Nursing	No Comments	No comments	Comment noted. No changes required.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Atrial Fibrillation Association	Agree	Atrial Fibrillation Association would like to confirm that they support and believe the proposed amends to Guidance No 197 by NICE is appropriate.	Comment noted. No changes required.
Sanofi	Agree	Sanofi agrees with the Institute's recommendation to adjust section 1.1. of TA197, as per the proposal in the table on page 5 of the consultation document, and that a 'holding' statement should be appended to the Institute's guidance webpage to reflect the changes to dronedarone's SmPC. We also agree that, in light of the new evidence and the nature of the changes to the licensed indication, dronedarone would in all likelihood still be considered cost-effective by a NICE Appraisal Committee and thus, we believe it would be most appropriate for TA197 to be transferred/incorporated directly into the on-going update to the Atrial Fibrillation Guidelines and not undergo a new assessment.	Comment noted. No changes required.

No response received from:

Patient/carer groups	General
• Action Heart • Afiya Trust	• Board of Community Health Councils in Wales • British Cardiovascular Industry Association

- Anti Coagulation Europe (ACE)
- Arrhythmia Alliance (AFA Affiliated)
- Black Health Agency
- British Cardiac Patients Association
- Counsel and Care
- Different Strokes
- Equalities National Council
- Grown Up Congenital Heart Patients Association
- Heart Care Partnership (UK)
- HEART UK
- Muslim Council of Britain
- Muslim Health Network
- Network of Sikh Organisations
- South Asian Health Foundation
- Specialised Healthcare Alliance
- Stroke Association

<u>Professional groups</u>

- Anticoagulation Specialist Association (ASA)
- British Association for Nursing in Cardiovascular Care
- British Association for Service to the Elderly
- British Association of Emergency Medicine
- British Association of Stroke Physicians
- British Atherosclerosis Society
- British Cardiovascular Intervention Society (BCIS)
- British Cardiovascular Society
- British Geriatrics Society
- British Heart Foundation
- British Nuclear Cardiology Society
- British Society for Haematology
- British National Formulary
- Care Quality Commission
- Commissioning Support Appraisals Service
- Department of Health, Social Services and Public Safety for Northern Ireland
- Medicines and Healthcare Products Regulatory Agency
- National Association of Primary Care
- National Pharmacy Association
- NHS Alliance
- NHS Commercial Medicines Unit
- NHS Confederation
- Public Health Wales NHS Trust
- Scottish Medicines Consortium

<u>Comparator manufacturers</u>

- Abbott Healthcare Products (Propafenone)
- Accord Healthcare (amiodarone, sotalol)
- Actavis UK (amiodarone, flecainide)
- Aurobindo Pharma (amiodarone, sotalol)
- Bristol Laboratories (sotalol)
- Bristol-Myers Squibb (sotalol)
- Hameln Pharmaceuticals (amiodarone)
- International Medication Systems (amiodarone)
- Meda Pharmaceuticals (flecainide)
- Mylan UK (sotalol)
- Sandoz (amiodarone)
- Sanofi (amiodarone)
- Teva UK (sotalol)
- Zentiva UK (amiodarone, flecainide)

• British Society for Haemostasis and Thrombosis (BSHT) • British Society for Heart Failure • British Society of Cardiac Radiology • Clinical Leaders of Thrombosis (CLOT) • Heart Rhythm UK • National Heart Forum (UK) • Primary Care Cardiovascular Society • Royal College of Anaesthetists • Royal College of General Practitioners • Royal College of Pathologists • Royal College of Physicians • Royal College of Surgeons • Royal Society of Medicine • Society for Cardiological Science and Technology • Society of Cardiothoracic Surgeons of Great Britain and Ireland • United Kingdom Clinical Pharmacy Association • Vascular Society <u>Others</u> • Department of Health • Somerset PCT Cluster • Swindon and Gloucestershire PCT Cluster • Welsh Government	<u>Relevant research groups</u> • Antithrombotic Trialists Collaboration (ATT) • British Society for Cardiovascular Research [BCS affiliated] • Cardiovascular Diseases Specialist Library (CVDSL) • Central Cardiac Audit Database • Cochrane Heart Group • Cochrane Peripheral Vascular Diseases Group • Cochrane Stroke Group • CORDA • European Council for Cardiovascular Research • MRC Clinical Trials Unit • National Heart Research Fund • National Institute for Health Research • Research Institute for the Care of Older People • Wellcome Trust - Cardiovascular Research Initiative <u>Assessment Group</u> • Assessment Group tbc • National Institute for Health Research Health Technology Assessment Programme <u>Associated Guideline Groups</u> • National Clinical Guidelines Centre

GE paper sign-off: Helen Knight, Associate Director – Technology Appraisals Programme

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