Response to: **ACD, Dronedarone for the treatment of Atrial Fibrillation**

Close date: 28th January 2010

Joanne M Jerrome – Patient / Carer Expert

Today's date: 25th January 2010

Has all the relevant evidence been taken into account?

In my opinion, not all of the relevant evidence has been taken into account. This is so for the following reasons:

i) An informed clinical expert who manages AF patients on a daily basis and with access and full understanding of all current treatments, was not present to highlight the importance of dronedarone in AF care, nor the significance of this new style of drug therapy.

ii) The evidence presented to the full committee, with all due respect, was done so by a non-specialist AF clinician (as admitted at the meeting) so the current limitations of AF management, drug options, procedure limitations, serious complications associated with current management options could not be conveyed.

iii) The early question 'Is this the miracle drug?' - led to an immediate negativity towards the ATHENA trial result. Yet this question was merely asking for an opinion, not a fact nor was it based on a claim from any of the trials, and as such not only should not have been aired by the presenting clinician, but also distracted Committee D from the actual results of the trial and what these results implied.

a) There is neither a cure nor any long term safe option for the treatment of Atrial Fibrillation. However, dronedarone is an innovative development. This is the first anti-arrhythmic medication (AAD) to be developed specifically for AF. It differs from current medication and as such cannot be considered in the same way as other, currently available AADs.

In the DIONYSOS trial amiodarone was expected to be more effect at controlling AF – and this was shown to be the case. However, the purpose of this trial was to see if there was an improved quality of life for AF patients as a result of using dronedarone. The results showed a significant (positive) difference in cardiac health and hospitalisation for those on dronedarone. To my understanding, this demonstrated that dronedarone was safer, better tolerated and more cost effective in quality of life terms.

b) Similar results were found when 'like' trials of dronedarone v placebo / sotalol v placebo were compared. While there was no significant difference in effectiveness to control episodes of AF, there was an overall improvement in cardiac health outcomes and rates of hospitalisations.

c) The ANDROMEDA trial was stopped early due to evidence showing the drug to be unsuitable for AF patients with severe heart failure, and it is now clear that dronedarone should not be used in this type of patient; what has to be balanced in this is that NO currently available AAD is suitable for the most ill/frail AF patient and that ALL AADs can be triggers for other cardiac events. For dronedarone, trials would suggest this is limited to those with severe heart failure, while all other AADs are known to have the potential to be harmful to others with AF.
d) Committee D failed to fully recognise that large number of AF patients are either unsuitable or unable to take existing AADs, either because of risks or side effects. Trial results indicate that this is only a problem for a few when taking dronedarone. Therefore, this new drug might be a new alternative to those currently left with no other choice.
e) While the ATHENA trial focused on older patients with more than one morbidity factor, the fact that dronedarone was suitable and effective in a large number of these individuals and was generally well tolerated, would suggest that it would be very suitable for younger, healthier patients facing long term medication.

Younger patients may be prescribed sotalol or flecainide as a first line AAD, but if, as is very common, these either cannot be tolerated or do not work, then this group of patients would NOT be suitable for long term use of amiodarone – leaving them with only catheter ablation as a choice – which is expensive not suitable for all, frequently needs repeating, not easy to access, only offered at a limited number of centres, and only has an average of between 50 -70% success rates. For this group, dronedarone would offer a new option and thus, new hope.

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

As explained in the first section, I do not think the summaries of the clinical effectiveness are reasonable.

When looking at cost effectiveness, I do not think the Committee has interpreted the evidence in full. I have limited understanding of the figures used, however I would make the following observations:

i) Dronedarone would not be used in all AF patients – it is estimated it would be suitable for approximately 55% of Paroxysmal AF patients, and of course, not all of these would need to be considered for dronedarone if current management approaches are successful.
ii) Quality of life improvements for those prescribed dronedarone would almost definitely be greater than on other medications – otherwise they would be on currently available medications.
iii) Reduced hospitalisation – which for AF is known to be very expensive, would also impact positively on the overall costs, and I do not see how these have been factored in.
iv) If dronedarone did not work, then the clinician would not keep the patient on the medication (and the patient would not want to remain on

dronedarone), so costs incurred by intolerance would be short and quickly cease. In the figures suggested in the ACD, this does not seem to have been recognised.

v) Result reported in the ATHENA were very significant in that they included a large number of patients and the results on all cause mortality and hospitalisation (24%) were shown to be significantly better with dronedarone – a cost saving for a health system, a much improved quality of life improvement for the patient. I do not think the Committee fully appreciated this.

Dronedarone could be considered for paroxysmal AF patients, without severe heart failure, who have little or no other choice, and it would only be used if the clinician felt it was a suitable option and then if the patient responded well to it. Therefore it would seem logical to expect dronedarone to be cost effective, or the drug is not prescribed any way.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

No. I strongly disagree with the preliminary ruling by Committee D on Dronedarone. I have already set out reasons for this and would reiterate:

i) Expert clinical evidence was missing at the meeting and should now be requested as essential for a future review meeting as this would inform more accurate cost studies.

ii) I believe the stated cost analysis by NICE is flawed and should be looked at again in light of HOW this new drug is seen to fit into AF care path-ways.

Furthermore, the experiences of the AF patient were not fully understood nor allowed to be presented.

For patients, AF is physically exhausting and emotionally draining. Paroxysmal AF patients face the uncertainty of never knowing when an episode might occur, its severity or how long it might last. These impacts on their physical, emotional and personal well being; too often AF disables a person leaving them isolated, too frightened to go out alone and feeling 'prematurely aged'.

There is a financial impact on life as well from the frequent medical appointments, travel to these and missed working days to limited job opportunities to forced early retirement and the need for long term care.

Current options are limited, do not suit all and for many, are not easy to access.

As to amiodarone, it may be good at reducing AF, but it is not good at keeping you alive. Its' side effects have a daily impact, and this can be the case for other AADs - sotalol and flecainide also need to be carefully monitored. I have heard patients comment: "The cure was worse than the cause.''

'Mild' side effects from other medications include: dizziness, aches and pains, rash, sun sensitivity and decreased energy. 'Severe' ones include: thyroid damage, liver problems, kidney problems and potential failure, lung and breathing problems or respiratory distress, vision problems such as halos, skin discoloration, severe hair loss, cognitive problems and speech loss and even death.

To this end I do not think the provisional recommendations to the NHS to deny approval of dronedarone are reasonable.

Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?

I believe the NICE ACD on dronedarone will discriminate

i) The first appraisal was flawed since it was not able to take into account all the evidence. In this I believe there may be discrimination against groups of patients.

ii) AF patients living in England and Wales who are unable to access or not eligible for procedures such as catheter ablation or cardioversion, will not be allowed access to assessment for dronedarone.

iii) NICE have not secured full patient and public participation in this process. The ACD is extremely complex and overly technical for a non-specialist reader.

iv) The published ACD does not include written responses from invited 'experts' in this way those AF patients and carers who did not attend the meeting have only Committee D's comments to follow. As already stated, these are extremely hard to understand and do not reflect all of the evidence.

v) Ruling that responses can only be via an on-line form, and later on a printed copy, has discriminated against those who do not have easy access to the internet (especially so for older people and AF is predominately a 65+ years condition).

vi) Again to reply within the set format even on paper is over daunting to those so very much affected by the ruling but who have no prior experience of NICE.

I urge NICE and Committee D to review its current ruling on dronedarone. Ensure that an expert clinical witness is able to attend the next meeting and that more time

is allocated to hearing presentations from the clinical experts and patient experts. Please give back to clinicians and patients the full options for care in AF and in doing so give back hope and quality of life to many AF patients who would benefit from dronedarone.