

Dear [REDACTED]

The following comments from [REDACTED] ([REDACTED] [REDACTED]) are submitted on behalf of the NCGC.

The data implied that adding ivabradine has a desirable effect on the morbidity and mortality in patients with heart failure due to left ventricular systolic dysfunction whose heart rate was over 70-75 bpm, either because they were not on beta-blockers due to contra-indication or due to intolerance; or because the patient were on beta-blockers but the dose could not be up-titrated further (usually due to low BP).

The report recognises that the main impact came from treatment of patients on no beta-blockers or on low doses of beta-blockers. This is a very important observation.

Based on this and on one of the important recommendations of CG 108, we are keen to emphasise:

- a. That there is no evidence of a comparison between beta-blockers and ivabradine in heart failure (the manufacturer made a comment that the effect of beta-blocker on heart failure is due to slowing down of the heart which is partly true but not entirely, as we know several BB were not as effective and we have CCB that slow the heart and are contra-indicated in heart failure), thus while ivabradine could be added to the treatment of patients with HF whose HR WAS 70-75 BPM OR ABOVE, we could not transform the sentence into ivabradine can be given as alternative first line therapy as there is no evidence for that at all.
- b. The practitioner and the patient are alerted, alongside the recommendation from this TA, to the main recommendation that challenged the past practice of assuming the presence of contra-indications to BB in certain groups who were thus prevented from deriving the benefits of BB therapy. These include the elderly, those with non-reversible COPD, those with diabetes mellitus, those with peripheral vascular disease and those with erectile dysfunction.

The health economic assessment made several assumptions that need to be challenged:

- a. It assumed that 50% of the HF hospitalisations in the UK will be under cardiology care, this is not correct. Audit data suggests no more than 30% at most are cared for in cardiology wards. This may or may not affect the calculations.
- b. Although the mean age of the patients in the trial and the sub-study was not higher than 60 years, for some reason the health economic study was based on a mean age of patients admitted at 78 years?

While the advent of Ivabradine in the treatment of heart failure due to left ventricular systolic dysfunction is a very important and welcome development, it would be fair to stress that its position is mainly as an add on agent in patients who are otherwise

optimally treated, and for the few who have an absolute contra-indication to beta-blockers and whose heart rate is over 75 bpm.

There is a statement towards the end of the report saying that ivabradine is the only non-surgical addition to the therapy beyond what is recommended in the guidelines. I am afraid this is inaccurate:

- a. While NICE rejected an application by the makers of eplerenone to re-consider its position following the publication of EMPHASIS-HF in November 2010; it remains true that had the GDG been allowed in May 2010 to consider the findings of EMPHASIS-HF then the algorithm for therapy would have reverted to what the GDG originally proposed in January 2010 (namely that the second line of therapy be an aldosterone antagonist), and that these agents could be given to patients in NYHA II.
- b. If by using non-surgical, the authors of the report did not mean non-invasive, then one has to also add that beyond the guidelines there is another important publication called RAFT study that altered the European guidelines for advanced pacing to include some patients with NYHA class II, provided they fulfilled stringent ECG criteria (QRS duration >150 msec and LBBB).

Regards

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NCGC