28th October 2020

Mr Tim Irish

Vice chair

National Institute for Health and Care Excellence

10 Spring Gardens

London SW1A 2BU

Dear Mr Irish,

1. Re: Final Appraisal Determination – Single Technology Appraisal, Tafamidis for treating transthyretin amyloid cardiomyopathy [ID1531]

The British Society for Heart failure would like to appeal against the Final Appraisal Determination for the above-mentioned technology appraisal on grounds 1a and 2.

Ground 1a: In making the assessment that preceded the recommendation, NICE has failed to act fairly due to the omission of representation by heart failure specialists.

1a. Failure to follow due process. Although the British Society for Heart Failure was listed in the Final Stakeholder's list as a consultee organisation and contributed to the original scope of the technology appraisal, and were invited to attend the first Appraisal meeting, the BSH were inadvertently excluded when the Appraisal Meeting was rescheduled to May due to the coronavirus pandemic. As the Society was no longer listed as a stakeholder the BSH was initially unable to even comment on the Appraisal Consultation document. When these errors were brought to the attention of NICE, we used the opportunity to explain the importance of including the input of a heart failure specialist at the next meeting. Unfortunately, the BSH were only permitted as observers in the final Appraisal Committee meeting.

Ground 2: The recommendation is unreasonable in the light of the evidence submitted to NICE

2.1 In the first page of the Final Appraisal Document, the reasons for not recommending Tafamidis are listed under the heading '**Why the committee made these recommendations'** as follows.

Tafamidis is the first treatment for ATTR-CM that aims to treat the disease. Evidence from clinical trials shows that it reduces deaths and hospitalisation from conditions affecting the heart and blood vessels compared with placebo.

- ***But clinical benefit varies across different types and stages of ATTR-CM.***
- ***Also, the measure used to assess how severe ATTR-CM is, has limitations. This makes it difficult to clearly identify who benefits from tafamidis and whether they should continue treatment.***
- ***The cost-effectiveness estimates are higher than what NICE normally considers an acceptable use of NHS resources. This is because there is not enough evidence that recommending tafamidis would reduce diagnosis delays and uncertainty about how long the treatment works after it is stopped.***

The BSH would like to appeal the basis of the decision on the first two of these three listed reasons.

1. ***'But clinical benefit varies across different types and stages of ATTR-CM.'***

   The NICE committee discusses the arguments for and against this issue on page 13 of this same Final Appraisal Document under the heading of **'The subgroup results are not suitable for decision making'.** As the committee have formally conclude that subgroup results would not be used for decision making due to lack of statistical power, it is inappropriate that this reason should be listed as a reason for not recommending Tafamidis.

   Furthermore, lack of statistically significant benefit in subgroup analysis for NYHA III and IV is well recognised in heart failure trials and this has not prevented approval of heart failure therapies by NICE in other technology appraisals.

2. ***'The measure used to assess how severe ATTR-CM is, has limitations. This makes it difficult to clearly identify who benefits from tafamidis and whether they should continue treatment.'***

The measure referred to is NYHA class. NYHA class is the measure used to identify individuals suitable for all NICE approved heart failure therapies in the last 10 years and is not a valid reason to fail to recommend a new therapy.

NYHA class is used as both a starting requirement (NYHA class > II for Ivabradine, Sacubitril Valsartan and Cardiac Resynchronisation Therapy) and as a 'not for therapy' rule (NYHA class IV = not suitable for Internal Cardiac Defibrillators).

In summary, the British Society of Heart Failure would like to highlight an inadvertent but important error in process that led to the exclusion of the Society from a large part of the decision-making process around this technology assessment. As Tafamidis is a treatment for heart failure patients, this has led to misconceptions which have persisted through to the final appraisal document, particularly regarding NYHA class and its use in day to day treatment decisions and its interpretation in the setting of heart failure trials.

Finally, the BSH agree with NICE that the cost savings due reduced diagnostic delays are difficult to cost due to insufficient data. For this reason, the BSH would support a delay in the final decision or an earlier review date at 12 months in order to allow more evidence on early diagnosis to be collected from the UK Early Access to Medicine's Scheme for Tafamidis.

The BSH would like to participate orally in future meetings for this Technology Assessment.

Yours sincerely,

[redacted]

[redacted], British Society for Heart Failure, on behalf of the Board of Trustees