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Sent by email to: [redacted]

[redacted],
[redacted]

Pfizer Limited,

Walton Oaks, Dorking Road,

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KT20 7NS

30 November 2020

Dear [redacted]

Re: APPEAL AGAINST THE FINAL APPRAISAL DETERMINATION FOR TAFAMIDIS FOR TREATING TRANSTHYRETIN AMYLOIDOSIS WITH CARDIOMYOPATHY

Thank you for your letter of 23 November 2020, responding to my preliminary views on initial scrutiny. This letter is my final decision on the points to be referred to the appeal panel. I will address only those points where you have submitted additional argument.

Ground 1(a): In making the assessment that preceded the recommendation, NICE has failed to act fairly

1.1 The Committee has failed to take into account relevant evidence or to explain why the diagnostic algorithm prepared by the National Amyloidosis Centre has not been accepted;

I stand by my view that the appraisal documents have to be considered in their entirety when assessing what the committee has taken into account or what explanation has been given. Your letter argues in reply that not all of the appraisal documents will be informative in that regard, for example a document prepared by a manufacturer. That may or may not be so, (after all, without reference to the manufacturers documentation we could not see, for example, what the evidence base was in the first place) but in any event it does not prove that no part of the appraisal other than the FAD can be considered. My point that the fairness of an appraisal process can only be assessed

with reference to the whole process must be right. The idea that this must mean stakeholders must guess what the committee's reasons were did not come from my letter.

Your additional arguments persuade me that this is not a fairness ground of appeal at all, but that it sits within reasonableness. You are clearly aware that the committee felt diagnosis might be challenging, and that appears to be a reason for the recommendation. You were obviously able to engage with that point and in my view it is unarguable that there was unfairness here. You are dissatisfied with the substance of the committee's decision but that sits within ground 2, and I will refer this point to the appeal panel under that ground.

1.4 The Appraisal Committee's conclusion that it would not consider starting and stopping rules for tafamidis based on the NYHA classification system even though the NYHA system has been used in previous NICE appraisals is unexplained and potentially discriminatory;

Thank you for your clarification that the point here is inconsistency only. Having considered the points in your letter I agree the point should go to an appeal panel. The essential point seems to be:

"… the Committee in this appraisal decided to reject use of NYHA classification as a basis for stopping rules, whereas NICE guidance following other appraisals has accepted use of NYHA, is a significant factor resulting in the Committee's negative decision. …, there is no justification for a different approach to that followed for treatments for other heart failure conditions and that is unfair."

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

2.3 The Committee's statement indicating that all patients with suspected amyloidosis are referred to the National Amyloidosis Centre for testing is incorrect;

I have considered the additional points you make, but I remain unconvinced this is a valid appeal point. The issues you raise seem to me to sit within your point 2.2, which I have already accepted as valid. I will not refer this point on in its own right, but you may make the same points as an aspect of ground 2.2.

2.4 The Committee's suggestion that biomarkers could have been used as an alternative to NYHA classification to assess disease stage and who would benefit from treatment is unreasonable;

I am still unpersuaded this is a valid appeal point. You are simply placing far too much weight on what seems to me to be a minor part of the FAD. Having explained that they had concerns about the NYHA classification, the committee went on to say that there was no alternative but to use it because there were no other data. It seems to me they were heading off a challenge in a reader's mind along the lines of "if the NYHA classification was so bad, why did you use it anyway". That cannot be unreasonable in itself and cannot have made the recommendation unreasonable (assuming the recommendation was otherwise reasonable, which is a question for the appeal panel.)

This is not a valid appeal point.

2.7 The Committee's conclusion that tafamidis has no impact on awareness of ATTR-CM is inconsistent with its view that other products are increasing awareness;

Although I have considered your additional arguments I still do not consider this a valid appeal point. The Committee have concluded that awareness of ATTR-CM has increased and will now be unaffected by the availability of tafamidis. That seems to me to be clearly a reasonable view to take. I am not persuaded that the availability of a licensed treatment (as opposed to unlicensed treatment or to best supportive care) has to drive increased awareness, which will depend on what clinicians see in their clinics, on the state of the scientific literature generally, as well as treatment options. I am not convinced that "there is little purpose in diagnosing a condition if there are no treatments available and diagnosis will make little change to management", because that proposition begs the question; until the condition is diagnosed the clinician would not know there were no treatments available. In any event I do not think clinicians approach diagnosis in this way. Indeed it seems the Committee view on awareness is if anything supported by some of your other appeal points that ATTR-CM is now well understood and readily diagnosable. I do not consider this a valid appeal point.

2.9 The assertion that Pfizer failed to make use of longer-term data in its extrapolation of treatment effects is unreasonable.

Thank you for your comments on this point. The correction of a possible slip of this sort is a matter for NICE's guidance executive (if the FAD gets to them after the appeal) rather than for me or the appeal panel. For that reason I cannot undertake that the change will be made but if the FAD it its present form goes forward for publication the Guidance Executive will be asked to look at changing this wording. On that basis I do not think this is a valid appeal point.

The valid appeal points therefore are: Ground 1; 1.2, 1.3, 1.4, and ground 2; 1.1, 2.1, 2.2, 2.5, and 2.6.

Many thanks

Yours sincerely

Tim Irish

Vice Chair

National Institute for Health and Care Excellence