8 February 2016

Dr A McKeon
Vice chair
National Institute for Health and Care Excellence
10 Spring Gardens
London SW1A 2BU

Dear Dr McKeon,

Thank you for agreeing the validity of our appeal points and the opportunity to respond to your letter dated 27 January 2016.

We have considered your comments on our 2.1 and have narrowed the sub-points as detailed below. We would be grateful if you would reconsider this as a valid appeal ground.

2.1 The AC and AG were unreasonable to conclude that prolonged-release tacrolimus is inferior to immediate release tacrolimus.

Astellas contends that the ACs conclusion that prolonged-release tacrolimus is inferior to immediate-release tacrolimus is unreasonable on the basis that the conclusion is:

1. Not based on any clinical evidence. Indeed the final conclusion is in sharp contrast with the position provided in FAD section 4.62 which clearly states that there '*were no consistent differences between immediate and prolonged-release tacrolimus'.* All evidence from RCTs comparing immediate-release tacrolimus with prolonged-release tacrolimus shows statistically significant non-inferiority in terms of clinical efficacy and side effect profile

2. Is diametrically opposed to the informed assessment already made by the Committee for Medicinal Products for Human Use ("CHMP") without any just reasoning. Regulatory Authorities consider efficacy and safety profile of these products to be therapeutically equivalent, as specified in the products' SmPCs.

Had the AG and AC used a modelling approach based on clinical equivalence of prolonged-release and immediate-release tacrolimus and also the correct prices (as per point 1a2 of our original appeal letter) then a substantially different conclusion is likely to have been drawn by the AC.

Yours sincerely

[redacted]
Medical Director

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