Responses from nominated experts by the British Association of Dermatologists on the briefing paper for thymosin beta-4 for epidermolysis bullosa

	Factual accuracy, particularly in relation to the current clinical need/burden of disease, and current UK practice/comparators	Proposed place of thymosin beta-4 in the treatment of epidermolysis bullosa, including any NHS service issues that may arise from its adoption	Any areas of clinical uncertainty or other research questions that should be addressed, including broader issues relating to the patient group, current management options, and NHS service delivery
Clinical expert 1	Mostly accurate. Page 2 background: keratin 14 not 15.	The main problem in EB is skin fragility which this treatment would not address. In milder types of EB, wounds usually heal. It is only in severe types that wounds fail to heal or recurrently break down. A topical therapy to enhance healing in such patients would be welcome. This would improve well-being, and reduce pain and need for dressings.	Currently there is no evidence that it works. The key results presented here seem to show that more wounds heal in the placebo group. There is no evidence of efficacy from other clinical situations either. Also, there is no evidence that it would reduce the risk of skin cancer, and it might increase it.
Clinical expert 2	Yes - agree.	Although not preventing chronic ulcers arising by reducing skin fragility, a treatment for recalcitrant wounds in EB would be very valuable and could, if effective, bring very tangible improvements to patient quality of life and considerable health economic benefits. The question is whether or not it actually works. Another question relates to the cost of such a treatment. This is not estimated in the summary provided.	This study compares the effect of TB4 or placebo in patients with different types of EB. It is an assumption that chronic wounds will behave the same in these different diseases and the actual numbers if broken down into subtype will be very small. The summary findings presented do not show efficacy; the number of wounds healed in TB4 vs. placebo is not significantly different. They state the percentage reduction in wound size for the lowest TB4 concentration vs. placebo but don't say how many patients there are in this particular treatment arm - presumably not many if N=22 for all 3 concentrations. Also, they don't give a p value - again probably because it isn't significant. Also, the mean wound size at the end was equivalent across all groups, placebo and TB4. So, does it work? I don't think we can say so from this. What is the data in other non-EB wounds?
Clinical expert 3	Agree.		From the data supplied there is no evidence that this topical therapy works even at day 56. I think itch is major problem in EB – does thymosin beta-4 have any effect on pruritis?
Clinical expert 4	Factually accurate in terms of need.	A need, not fulfilled, by the data presented.	The summary, if to be believed, seems to imply that the placebo resulted in healing in more patients than with the active ingredient. Yet wound size supposedly shrank more in treated than untreated. The stats are not here to support this apparent assertion. Seems to imply that placebo is better…? I do not believe the data presented are useful or contributory for a phase 2 trial, which should principally address dose optimization and safety.