Additional Information provided by the External Assessment Centre during preparation of the Assessment Report Overview

1. Assessment of the statistical analysis of the results of the Hampton et al. 2009 study (see sponsor submission Appendix 5 page)

The EAC found the reporting of the original study and of the further analysis to be of such poor quality it was difficult to understand exactly what the authors had done. It was difficult to understand the rationale for the test chosen and statistical results were reported poorly. The EAC's understanding of what was done is given below, but may reflect poor reporting.

10 patients were included as heel cases and 18 as sacrum cases with some overlap. All had grade 1 tissue damage over the sacrum and one or two heels, but no further information on the subjects was given. For the heel cases, the right but not the left heel was treated with Parafricta. No description of the right and left heels at baseline was provided, but results refer to "normal" and "treated" heel. We do not know how many right heels had grade 1 ulcers.

Results were expressed as pixel intensity spectra derived from an ultrasound scan (both heels scanned for heel patients). Normal skin was scanned to provide a standard for comparison. Mean spectra for normal skin, time 0, time 2 weeks and time 4 weeks were calculated, and these mean spectra were then expressed as cumulative % distributions. This allowed the authors to calculate 2 sample Kolmogorov-Smirnov tests to assess whether these distributions were statistically different. This test assesses difference on the basis of the maximum difference between two cumulative distributions and does not assume any particular distributional shape.

This statistical approach was incorrect on a number of counts.

1. A two sample test was inappropriate, as each patient has two heels which were compared, so a paired sample statistical test should have been used.
2. The cumulative distribution used for the K-S test should be based on a single observation for subject (for example a cumulative distribution of a pressure ulcer score could have been constructed). The cumulative distributions here seem to be based on averaged distributions for each subject. An alternative summary measure such as the area under the curve should have been used.
3. Multiple tests at different time points are presented. Ideally, a repeated measures analysis should have been used, but the small sample would have been a limitation.

Similar considerations apply to the sacral results, and this study additionally was uncontrolled, as normal skin cannot be considered an adequate control site.

2. Additional information relating to economic evidence

The EAC confirmed that

The time horizon for the hospital model was limited to the in-patient stay in the Smith and Ingram study (see assessment report and was up to 4 months.

The sensitivity analysis of the community model investigated the impact of assuming Parafricta was 50% less effective, this meant the prevalence ratio was changed from 0.37 to 0.685 in the model.

In the revised community model, the prevalence ratio used was based on the adjusted mean length of stay values calculated by the EAC and a value of 0.53 was obtained.