Reviewer's report

Title: Tobramycin exposure from active calcium sulfate bone graft substitute

Version: 2 Date: 5 December 2013

Reviewer: Cornelia Landersdorfer

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Major Compulsory Revisions

1. Two different amounts of Osteoset T (10 and 20 g, which correspond to 262 and 524 mg tobramycin) were studied. Simulations were performed for 262, 786 and 1310 mg tobramycin. It is not clear how the simulations for 786 and 1310 mg tobramycin were performed, given that the bioavailability of tobramycin from Osteoset T depends on the amount of Osteoset T implanted. The relationship between amount of Osteoset T and bioavailability is not known, therefore the bioavailability of 786 and 1310 mg tobramycin is not known.

2. The data and visual predictive checks for both studied doses need to be presented, e.g. Figure 1a: 262 mg dose and Figure 1b: 524 mg dose.

3. Figure 1: It is not clear why the predicted concentration time profile for the 95th percentile (dashed line) is very flat starting at 72 h although a 1 compartment model was employed.

4. It should be reported how the simulations were conducted, including the number of virtual profiles that were simulated for each dose and renal function.

5. The results of the simulations should be reported in more detail.

Minor Essential Revisions

1. Introduction: The expression ‘concentration levels’ should be replaced by ‘concentrations’.

2. Drug assay: The assay performance parameters (precision, accuracy) of the runs in which the samples were analysed should be reported.

3. A number of samples had concentrations below the quantification limit and it is not reported how those were treated in the population analysis. Not taking into account BQL samples can potentially bias the analysis.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.