Norgine Clarification on Factual Inaccuracies in the ERG Critique of Norgine Addendum to the NICE STA on Rifaximin-α 550mg

Page No	Section of ERG Critique	Relevant Text	Norgine Clarification
Page 11	Literature Searches	1) Updated Literature searches 2) Targeted Mortality Search 3) Adverse Event Search	1) Norgine can confirm that the updated searches supersede those previously submitted. 2) A mortality search was not a requirement for the submission. The targeted literature search on mortality was undertaken as additional evidence in August 2013 and was run from 1990 onwards. Due to time constraints a decision was made to focus on Medline and Embase; as these databases would normally include the majority of literature available. 3) Adverse events – As per Norgine's response to the ERG's clarification questions in April 2013, a separate search for adverse events was not deemed necessary outside of the clinical, QOL or cost-effectiveness systematic reviews as data on adverse events were included in the clinical trials reported in these searches.
Page 12 & 23	Model Structure	Subsequent HE episodes considered as a unique event (i.e. cardinality of events was ignored in the analysis) thus modelled in a single health state.	Norgine sought guidance on this from the NICE technical team who made it clear that a structural change to the economic model would be unacceptable as additional evidence. Thus, a decision was made to remain true to the original structure submitted and only make changes to the input parameters to the model.
Page 28	ERG critique of the method applied in the mortality section of the addendum - 2nd Paragraph	Furthermore, it was not demonstrated in any manner (neither in the Addendum report nor in the excel model) how the probability of death in both overt states was calculated. Presumably these were obtained as a ratio of the number of events (i.e. deaths) observed at the end of RFHE3002 for patients in the overt and the total number of patients in the overt state over the 2-year study period	This paragraph infers a single mortality calculation was used not differentiating between O_1 & O_2. This is incorrect. Two separate mortality proportions were calculated. Please see: • 4.3.4.2 Overt (O_1) Mortality Calculation • 4.3.4.4 Subsequent Overt (O_2) Mortality
Page 30	ERG critique of the method applied in the mortality section of the addendum - 1st Paragraph	Overall mortality in the placebo and in the rifaximin arm at year 5 show that approximately 55% of patients are dead in the rifaximin arm while 45% remain alive in the placebo arm	These values are incorrect and should read 52% alive rifaximin, 44% alive placebo (47.7% dead rifaximin / 55.5% dead placebo). Please see Addendum section 4.3.6 – table 11.