Review of Technology Appraisal 67: Amantidine, oseltamivir and zanamivir for the prophylaxis of influenza

GSK comments on the Assessment Group Report

Pages 103/4, 150	Extrapolation of the data to sub-groups that have not been studied ▪ We appreciate that the Assessment Group had to make the best use they could of available data, but we have concerns about the analysis of cost-effectiveness in sub-groups where no actual data, or no specific data, on effectiveness exists. In these sub-groups, cost-effectiveness has been calculated using data partly or wholly from other sub-groups which may not be relevant. Predicted cost-effectiveness of anti-viral therapy and comparisons made between antivirals in these sub-groups are therefore subject to considerable uncertainty, which is not fully reflected in the way the cost-effectiveness results are presented. ▪ In particular, the effectiveness of zanamivir in post-exposure prophylaxis for children and the elderly (healthy and at-risk) is assumed to be similar to that seen in studies in mixed households. In these studies, households were predominantly healthy adults, with some healthy children and very few elderly or at-risk. ▪ For oseltamivir, the effectiveness of post-exposure prophylaxis in the elderly (healthy and at-risk) is assumed to be similar to that seen in studies in mixed households which again were predominantly healthy adults. ▪ The effectiveness of seasonal prophylaxis with either zanamivir or oseltamivir in children is assumed to be similar to that in adults.
Pages 174-192	Representation of uncertainty in cost-effectiveness ratios ▪ In nearly all of the results presented, one anti-viral is found to dominate the other. Dominance is a strong finding, and seems unwarranted given the underlying weakness of the evidence base in some sub-groups and the heterogeneity in trial data used. ▪ Although indirect comparisons used a common comparator (placebo), this cannot control for differences in the countries included and circulating strains of influenza, resulting from the fact that studies were international and conducted in different years. Therefore, in the absence of head-to-head data, differences in effect should be interpreted very cautiously. ▪ In particular, in post-exposure prophylaxis in adults and the elderly, oseltamivir is found to dominate zanamivir based on the relative effect seen in mixed households. As mentioned above these studies included few elderly subjects, but more importantly, relative cost-effectiveness is based on a very small difference in effect, with relative risk (RRs) of 0.21 for zanamivir and 0.19 for oseltamivir. Also, the 95% confidence interval for the RR with zanamivir (0.13-0.33) is entirely within that for oseltamivir (0.08-0.45). Given the uncertainties with comparisons between trials described above, these results suggest similarity of effect between zanamivir and oseltamivir, or at least they do not provide evidence of a difference. ▪ In post-exposure prophylaxis in children, zanamivir is found to dominate oseltamivir. This is based on an indirect comparison of the effectiveness of zanamivir in mixed households (mainly healthy adults) with oseltamivir in children, and therefore it is not clear that this represents a real difference in effect in children. 279-302 ▪ Although the Assessment Group has undertaken extensive probabilistic sensitivity analyses, these do not reflect the uncertainty introduced by assuming similar effect s across different sub-groups and the heterogeneity in trials discussed above
Page 21	Conclusion ▪ Given the uncertainties described above and noted in the report, the most plausible assumption on the available evidence, is that zanamivir and oseltamivir are of similar effectiveness, and unless there are differences in costs, are also similarly cost-effective.