Health Technology Appraisal
Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza (including a review of existing guidance no. 67)
Appraisal Consultation Document

Comments from the Health Protection Agency
9 June 2008

Comments from the HPA relating to the appraisal consultation document

i. Do you consider that all of the relevant evidence has been taken into account?

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Appendix B: Apart from input from the Health Protection Agency, there appears to have been no formal input from the microbiology/virology/infectious disease specialty groups.

iii. Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

Page 3, Section 1.1, 4th bullet and throughout the document (see also page 26, Section 4.3.4): It is somewhat misleading to state that the surveillance scheme threshold is used to determine "whether influenza virus is circulating in the community." The threshold demarcates (as correctly stated in Section 1.6, page 5) "normal seasonal activity." However, when the GP consultation rate falls below this level, there are other data (as detailed in the HPA Weekly National Influenza Report) that clearly indicate that the influenza virus is "circulating in the community."

The NICE document suggests that no alternative method was proposed for determining whether influenza virus was circulating in the community. This is not the case. The HPA view, and supported by the recent action by the NPHS Wales (which re-issued, on behalf of the Welsh Assembly Government, the recommendation to use anti-virals in the light of the circulation of influenza B late in this season), is that the national health protection bodies in England, Wales, Scotland and Northern Ireland should determine whether or not influenza virus is circulating in the community based on their range of surveillance indicators. Although it would be convenient and administratively simpler if there were a routinely available single numerical indicator to indicate reliably the circulation of influenza viruses in the community, no such single indicator exists. The advice to the respective Health Departments, to advise practitioners on whether the period when it was appropriate to prescribe influenza antivirals had arrived, should be provided by the health protection bodies conducting the influenza surveillance.

Page 26, Section 4.3.4. Strong consideration should be given to replacing "whether influenza virus is circulating" with "normal seasonal activity."

Page 4, Section 1.3: Not included in this list are other groups for whom vaccination is recommended, such as health care workers and caregivers of persons at risk. In certain situations, might post-exposure prophylaxis be considered; for example, an

unvaccinated health care worker or caregiver of a person at risk who is a close contact of a person with influenza?

Page 4, Section 1.5: Persons at risk who were vaccinated after circulation of influenza virus has begun may not be effectively protected for at least 2 weeks or more and should be considered for inclusion in this group.

Page 4, Section 1.4: Close contact might reasonably be expected to occur in closed settings other than households, such as residential institutions, boarding schools, and the like. Depending on the nature of the prevalent influenza illness, there may be strong public health reasons to extend prophylaxis to other residential groups. A virus, for example, causing particularly severe disease in children might prompt a greater level of protective action in a boarding school outbreak. As written, it appears overly restrictive.

Page 5, Section 1.6: Only residential and nursing homes are cited; similar to the comment for Section 1.4, this may be too restrictive and importantly excludes other closed settings such as prisons as well as hospital settings where nosocomial transmission has been well documented.

Page 25, Section 4.3.2: As noted above, the at-risk groups are not defined exactly as they are for current vaccine recommendations.

Page 31, Section 4.3.11: Use of antivirals for outbreak settings is sensible, but consideration should be given to making language somewhat less restrictive (similar to previous comments) as there may be setting other than “long-term residential or nursing homes” where prophylaxis would be appropriate.

Comments from the HPA relating to the Evaluation Report

Overview:

Page 15, para 2 and page 29, Table 29: Probability that an ILI is influenza

Restricting use of RCGP data to only those weeks when the consultation rate is above 30 per 100,000 results in a self-fulfilling bias. Page 143 describes Table 29 as data for "weeks when influenza was known to be circulating in the community." However, as previously articulated in the HPA submission to NICE, influenza is clearly circulating in the community in the time before and after the 30/100,000 threshold is attained. In 2007/08 for several weeks the proportion of specimens positive for influenza was equivalent or greater to the proportion positive when the threshold was attained http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947379134.)

Assessment Report

Page 145, Table 31: The title of the table is misleading as surveillance reports refer to the period when the consultation rate is >30 per 100,000 but less than 200 per 100,000 as "normal seasonal activity."

Page 252, Appendix 6: It would be helpful to provide more specific information as to why studies were excluded if they were "not in line with licensed indications." For example, if studies were excluded because prophylaxis was not initiated within 48 hours, the findings might still be of interest. As is noted by Roche's response (viii): "Whilst it is well acknowledged that treatment within 48 hours is important in the treatment setting the impact of this treatment rule upon efficacy in the PEP setting is less certain." Further acknowledgment of the uncertainty about the applicability of 48 hours in noted on page 8 of the British Thoracic Society response.