

Comments on behalf of The British Thoracic Society on Technology Assessment Report Commissioned by the NHS R&D HTA programme on behalf of the National Institute for Health and Clinical Excellence: Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza (including a review of existing guidance no. 67)

This is a well written and balanced review of the field. A small number of general and more specific comments/concerns are detailed below.

General Comments

- 1) The document contains broad conclusions and recommendations over the use of Neuraminidase inhibitors (NI) in at risk individuals. The trials referred to in this review were conducted on elderly individuals. The term *at risk* also includes individuals with immunodeficiency for example those on immunosuppressive drugs or undergoing chemotherapy. These individuals are at particularly high risk from influenza, and do not clear the virus as quickly as healthy individuals. Consideration should be given to relaxing the restrictions on the use of NI extrapolated from the elderly probably should be relaxed for immunodeficient individuals (particularly the 48 h time limit).
- 2) The levels of influenza activity seen in the last 10 years are very low in historical terms (lowest for >100 years). It is not clear whether this is because the influenza viruses are becoming less virulent or whether herd immunity has improved. The trials on the efficacy of the NI (but not amantadine) were carried out in winters with minimal influenza activity, and it is perhaps not surprising that only modest results were obtained from the trials. The current situation with minimal influenza activity may change and with a return to more normal influenza activity associated with regular winter epidemics, either secondary to a substantial antigenic drift or shift. Under these circumstances the guidance given restricting the use of NI will need to be rapidly reviewed and this perhaps should be reflected in any recommendations by NICE

Specific Comments

- 1) *P12 line 4 and P22 line 4 "influenza virus"*. Strictly influenza viruses (as A & B & C are distinct viruses).
- 2) *P12 Line 5 "Influenza illness is usually self limiting in otherwise healthy people"*. As serious influenza complications including death can occur at any age in previously fit individuals, a statement such as "though complications can occur in previously healthy individuals".

- 3) *P22 6 lines from bottom complications* – as above.
- 4) *P13 2.4* Some reference to whether the trials were conducted during a pandemic, epidemic or normal seasonal activity would be helpful, and would put the relative clinical efficacy of Amantadine and the NI in context.
- 5) *P23 end of section on prognosis, complications and mortality.* A statement outlining that we are currently experiencing very low levels of influenza activity would be helpful.
- 6) *P24 line 15 regarding pandemics,* there is evidence that the antigenic shifts can occur in seasons preceding the pandemic.
- 7) *P24 end of section on influenza strains and subtypes* There is debate as to the original source of the 1918 pandemic virus with Prof. Oxford and colleagues making a good case for its emergence in France a few years earlier.
- 8) *P25 line section on epidemics.* This should start “In the UK” or “In the northern hemisphere”.... As Influenza activity can be seen in airline travellers out of the UK season. Influenza outbreaks can occur out of season in closed communities and this should be taken into account in the NICE guidance.
- 9) *P26* Why does Wales have a higher threshold for influenza like activity? Will this be reflected in the guidelines for the drugs use?