Zanamivir for the treatment of influenza in adults: a systematic review and economic evaluation

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Executive summary

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Executive summary

Background

Zanamivir is a neuraminidase inhibitor specifically designed to interfere with the replication of influenza A and B viruses. It, therefore, has the potential to be useful in the treatment or prevention of influenza. It is currently licensed for the treatment of influenza in people aged 12 and over with symptoms of influenza when influenza is circulating.

Influenza is a common condition affecting all age groups. It occurs during the winter months and causes significant morbidity and increased mortality. The elderly and those with pre-existing medical problems, such as heart disease and renal disease, are particularly at risk of suffering severe disease or developing complications.

The policy in the UK is to vaccinate at-risk individuals. Otherwise-healthy adults with influenza are encouraged to stay at home and take over-the-counter medications for symptomatic relief. At-risk adults with influenza usually receive non-influenza-specific supportive care. Amantadine, an oral antiviral agent effective for treating influenza but which can cause adverse GI effects, is also available.

Questions addressed by this review

(1) How effective is zanamivir in shortening the time-course, reducing the severity of illness or preventing death in otherwise healthy adults with influenza?
(2) How effective is zanamivir in shortening the time-course, reducing the severity of illness or preventing death in adults at risk of suffering severe adverse outcomes from influenza?
(3) What is the frequency and severity of adverse effects associated with the use of zanamivir in both healthy and at-risk adults?
(4) What is the cost-effectiveness of zanamivir for the treatment of influenza in healthy and at-risk adults?

Methods

A systematic review of randomised controlled trials and economic evaluations addressing the above questions was undertaken and a UK model of cost-effectiveness developed.

Results

Effectiveness in all adults

The results of ten trials were included in the review of effectiveness in all adults. Where possible, they were combined in pooled analyses.

Inhaled zanamivir 10 mg twice daily for 5 days (the licensed dose) was found to reduce the duration of symptoms of influenza by 1 day (95% confidence interval (CI), 0.4 to 1.7) from about 6 to 5 days and the time to return to normal activities by 0.5 days (95% CI, –0.4 to 1.5) from about 7 to 6.5 days (not statistically significant) in the intention-to-treat population (ITTP). In the influenza-positive population (IPP), the treatment effect was marginally larger but this was not significantly different from that in the ITTP.

Effectiveness in at-risk adults

The results of seven trials contributed to the review of effectiveness in at-risk adults. Only one trial recruited an exclusively at-risk population. Six trials in all adults provided data from at-risk subgroups. The pooled analysis was based on 371 in the zanamivir group and 392 in the placebo group.

Inhaled zanamivir 10 mg twice daily for 5 days was found to reduce the duration of symptoms of influenza by 1.16 days (95% CI, 0.13 to 2.19) from about 8 to 7 days in the ITTP and by 1.67 days (95% CI, –0.02 to 3.37) in the IPP. The data did not have the power to demonstrate any differences in hospitalisation or death rates for either group. The drug had a similar adverse event profile to the placebo group.

Economic evaluation

Zanamivir costs £24 for a 5-day course of treatment. Only one cost-effectiveness analysis was

found in the published literature, which was for use in at-risk patients. Although the analysis followed established methods, it was based on one trial with only 37 participants in the zanamivir arm, and some of the assumptions did not reflect the true clinical situation. Therefore, we had limited confidence in its conclusions.

We derived UK-based estimates of cost-effectiveness using all data available. The base-case incremental cost per day of symptom avoided was £50 for all patients when influenza is circulating (i.e. the licensed indication) and £42 for at-risk patients when influenza is circulating. The incremental cost per quality-adjusted life-year (QALY) gained was £65,000 for all adults when influenza is circulating (i.e. the licensed indication) and £54,000 for at-risk adults when influenza is circulating (although this was based on a difference in effect that was not statistically significant).

Sensitivity analyses showed these results to be highly sensitive to a number of parameters. The cost/QALY varied from £15,000 to £117,000/QALY if used in at-risk adults and £18,000 to £341,000/QALY if used in all adults. A significant reduction in price of the drug (to £8) brought the incremental cost-effectiveness ratio (ICER) to £21,000 for all adults when influenza is circulating. Assuming a very large gain in quality of life (QoL) from treatment (influenza utility = 0, no influenza utility = 1) reduced the ICER to £18,000 for all adults when influenza is circulating. Changing the gain in health-related QoL for those at risk produced ICERs that ranged from £15,000 to £54,000, i.e. from a cost/QALY that compares favourably with many other treatments currently used in the NHS to one that has been seen under some circumstances as poor value for money. QoL data collected in a number of trials was not made available. Given the importance of QoL changes for determining the ICERs, empirical patient-level information is vital.

Conclusions

The evidence base for at-risk adults has greatly increased since this product was first reviewed by the National Institute for Clinical Excellence. The data available suggest that it may prove useful when used judiciously in at-risk patients. It will be important to monitor its use and incorporate new trial evidence as it becomes available to confirm this.

Publication

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