

Peramivir for the treatment of uncomplicated influenza

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Peramivir (Alpivab) is an intravenous antiviral medicine licensed for the treatment of uncomplicated influenza in adults and children from the age of two years. This article examines its efficacy and adverse effects.

NICE guidance on the treatment and prophylaxis of influenza has not been updated since 2009. The dopamine agonist amantadine is not recommended for treatment or prophylaxis of flu.^{1,2} The neuraminidase inhibitors oseltamivir (oral) or zanamivir (inhaled) are recommended as treatment options when national surveillance schemes indicate influenza virus A or B is circulating, the patient is in an 'at-risk' group (ie due to a chronic disorder such as asthma, heart disease or diabetes) and the patient presents within 48 hours (36 hours for zanamivir in children) of symptom onset and can start treatment within that period.¹ Treatment may also be offered at other times to 'at-risk' individuals living in long-term residential or nursing homes and a localised outbreak of flu is confirmed.

Oseltamivir and zanamivir may reduce symptom duration by 1–1.5 days and can reduce the risk of complications from influenza in at-risk individuals. These agents may also be offered as post-exposure prophylaxis to exposed individuals who haven't been vaccinated and otherwise meet the criteria for treatment.² In 2017, about 17,000 prescription items for oseltamivir were dispensed in primary care in England (and 64 for zanamivir).³

Peramivir (Alpivab) is a neuraminidase inhibitor first introduced in Japan in

KEY POINTS

- Peramivir is a neuraminidase inhibitor for the treatment of uncomplicated influenza in adults and children aged two or older
- It is administered as a single intravenous infusion over 15–30 minutes
- Compared with placebo, peramivir reduced the duration of flu symptoms by almost one day
- In another trial, it was non-inferior to oral oseltamivir for reducing symptom duration
- There is a lack of evidence of its efficacy in patients with influenza B or complicated influenza
- Adverse effects are generally mild, and include diarrhoea, nausea, decreased neutrophil count, proteinuria and increased liver enzymes

2010, which has recently been licensed in the EU for the treatment of uncomplicated influenza in adults and children aged two or older. NICE suspended a planned appraisal of peramivir for the treatment of influenza when the company failed to make a submission within the specified timelines.

Administration

Peramivir is administered as a single intravenous infusion over 15–30 minutes within 48 hours of the onset of influenza symptoms at a dose of 12mg/kg for children aged two years and over and <50kg body weight, and at a dose of 600mg in adults and adolescents aged >13 years, and children ≥50kg body weight. No dose adjustment is recommended for older patients or people with hepatic impairment.

The dose should be reduced in patients with renal impairment, depending on their absolute glomerular filtration rate (GFR). Peramivir is largely eliminated renally and the dose should be reduced in people with moderate or worse impairment of renal function (GFR <50ml/min), in accordance with the summary of product characteristics. Viral strains that are resistant to oseltamivir due to the H275Y mutation are also resistant to peramivir.

Efficacy

Clinical trials included few patients with confirmed influenza B infection or complicated influenza. Pivotal evidence for peramivir comes from one randomised, double blind trial in 296 adults during the 2008/2009 influenza season.⁴ Patients aged 20–65 years (mean age 34 years; 8% aged ≥50 years) with fever and moderate to severe systemic and respiratory flu-like symptoms who tested positive for influenza virus antigen received peramivir 300mg or 600mg or placebo within 48 hours of symptom onset. All but three patients had influenza A. The primary endpoint was the time to sustained alleviation of symptoms according to patients' diary records.

The median duration of symptoms after treatment with peramivir was 59 hours at 300mg and 60 hours at 600mg; this was significantly less than the 82 hours in placebo recipients. Symptom scores were significantly lower with both doses of peramivir than placebo after one day and for five days. The median time to recovery of normal temperature was 30 hours with 600mg peramivir and 42 hours with placebo. Time to resumption of normal activities was approximately 1.6 days shorter with peramivir than placebo.

Peramivir has also been assessed in a non-inferiority trial with oseltamivir (n=1099; 70 with influenza B).⁵ The

median time to alleviation of symptoms was about 80 hours with both drugs, with median times to resumption of usual activity of 156–196 hours with peramivir and 171 hours with oseltamivir.

Another study evaluated peramivir or oseltamivir in 108 children (mean age 9.9 years, range 2–18), of whom 75 were included in the intention-to-treat analysis.⁴ This study was not primarily designed to compare efficacy, with only 16 children assigned to treatment with oseltamivir and 59 children assigned to peramivir. Flu symptoms were alleviated after a median of 76 hours with peramivir and 100 hours with oseltamivir. Influenza virus titre was positive at baseline in 68 children. After three days, the positive titre was lower in children treated with peramivir (51% vs 77%); there was no difference after seven days. The outcome was not affected by age.

Adverse events

Adverse events associated with peramivir in clinical trials were mild and occurred with a frequency similar to that reported with placebo. Adverse events were reported more frequently in older people (age >65 years: 72%) than in younger adults (49%). The most frequently reported events considered to be treatment-related were diarrhoea (4.5%), nausea (2.1%), decreased neutrophil

count (1.8%), proteinuria and increased liver enzymes.⁴

References

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Declaration of interests

None to declare.

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