

Oseltamivir is widely available, primarily in generic formulations. Oseltamivir is listed as a complimentary medicine on the WHO Essential Medicine List (REF). Oseltamivir is an oral medicine and is well absorbed when given enterically via an oro-gastric or naso-gastric tube.

Justification

Data from clinical trials are very limited for oseltamivir in patients with severe influenza virus infection. The GDG inferred that for severe seasonal influenza virus infection, the threshold for use of oseltamivir treatment would be a reduction in mortality of 0.3%. For both seasonal influenza and zoonotic influenza (novel influenza A viruses associated with high mortality) it is very uncertain if oseltamivir increases or reduces mortality or ICU admission.

The GDG inferred that the threshold for use of oseltamivir treatment of severe influenza virus infection would be a reduction in duration of hospitalization by 1 day for seasonal influenza. While again oseltamivir was above this threshold the evidence was assessed as low certainty and thus we are uncertain of whether oseltamivir increases or reduces hospitalization.

However, previous recommendations by WHO [54] recommended to use oseltamivir in severe patients and the GDG, after significant deliberations, did not desire to change direction of recommendation without any new evidence to the contrary. Thus, as patients with severe influenza have a substantial risk of dying and given the likelihood of minimal adverse effects, even with only very low certainty evidence, the GDG judged that the majority of patients would choose to use the drug because of the possibility of benefit. The GDG noted that there is considerable experience in using oseltamivir for patients with severe influenza. The GDG also acknowledged that there are ongoing trials in severe influenza  infection testing antivirals and that this recommendation should be re-evaluated once more clinical trial data emerges.

Applicability

Oseltamivir can be administered to pregnant women, and children including neonates.

Clinical question/ PICO

Population: Patients with severe influenza
Intervention: Oseltamivir
Comparator: Standard care/placebo

Summary

The evidence regarding oseltamivir versus placebo or standard care was informed by 2 RCTs, which enrolled 104 patients with severe illnesses (studies provided the direct comparison for any outcomes of interest). One study enrolled pediatric patients (0–9 years), and one study enrolled adults (18+ years). Studies did not enroll patients with zoonotic influenza. The status of vaccination for the influenza virus was not reported. One study enrolled patients with mixed types of influenza virus infections, such as H1N1, H3N2, and type B. One study did not report the types of influenza viruses.

The appendix summarizes study characteristics, risk of bias ratings, and effect estimates by outcome for oseltamivir versus standard care.

For patients with severe influenza, the GRADE Summary of Findings table shows the relative and absolute effects of oseltamivir compared with placebo or standard care for the outcomes of interest, with certainty ratings, informed by the NMA.

Subgroup analysis

Four pre-specified subgroup analyses were requested by the GDG:

Influenza type: seasonal, zoonotic, pandemic influenza viruses

Confirmed vs. suspected infection

Age: children < 2 years, children vs. adults and adolescents vs. older adults (≥ 65 years)

Patients at increased risk of poor outcomes vs. not

Sufficient data were unavailable to inform pre-specified subgroup analyses.

