Use of neuraminidase inhibitors in out-patient settings

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2. Scope

2.1. For consideration of empiric treatment against influenza at out-patient settings.

3. Background

3.1. Based on the latest epidemiological and clinical assessment, the Taskforce on Clinical Management of Infections recommends the following approach on empiric antiviral therapy against influenza.

4. General Consideration

4.1. Clinical judgment, based on the patient's disease severity and progression, presence of risk factors for complications of influenza, time since onset of symptoms, and likelihood of influenza, is important to consider when making decisions on antiviral treatment.

4.2. Early antiviral treatment may reduce the risk of complications and improve clinical outcomes of influenza (e.g., pneumonia, respiratory failure, and death). Antiviral treatment is recommended as early as possible for any patient with confirmed or suspected influenza who:

(i) has severe, complicated, or progressive illness; or

(ii) is at higher risk for influenza complications.

4.3. The greatest benefit is when antiviral treatment is started within 48 hours of influenza illness onset. Antiviral treatment may still be beneficial in patients with severe, complicated, or progressive illness, when administered more than 48 hours from illness onset.

4.4. While the followings are reported as risk factors for complications of influenza in literature, a case-by-case assessment is needed for indication of antiviral therapy:

4.4.1. Children younger than 2 years old;

4.4.2. Adults 65 years and older;

4.4.3. Persons with significant comorbid conditions

(i) chronic pulmonary (including asthma),

(ii) cardiovascular (except hypertension only),

(iii) renal,

(iv) hepatic,

(v) haematological (including sickle cell disease),

(vi) neurological and neurodevelopmental conditions,

(vii) metabolic disorders (including diabetes mellitus);

4.4.4. Persons with immunosuppression, including that caused by medications or by HIV infection;

4.4.5. Women who are pregnant or post-partum (within two weeks after delivery);

4.4.6. Persons younger than 19 years of age who are receiving long-term aspirin therapy;

4.4.7. Persons who are morbidly obese (body-mass index ≥40);

4.4.8. Residents of nursing homes and other chronic-care facilities.

5. Regimen and adverse events of oseltamivir (Tamiflu®)

5.1. For adult and children 13 years old or above:

(i) Normal dosage is 75mg BD for 5 days.

(ii) Dosage adjustment is required in patients with renal impairment or undergoing dialysis. Dosing recommendations have been proposed for patients with creatinine clearance < 10ml/min or undergoing routine renal dialysis treatment, but are based on limited pharmacokinetic data.

Table 1. Dosage adjustment of oesltamivir for renal impairment

CrCl (ml/min)				**Patients undergoing dialysis**
>60 - 90	>30 - 60	>10 - 30	< 10	CAPD: 30 mg single dose HD: 30mg after every HD cycle
75mg BD	30mg BD	30mg daily	No data; consider 30mg single dose	

CAPD: continuous ambulatory peritoneal dialysis; CrCl: creatinine clearance; HD: haemodialysis

5.2. Dosage for children aged 1-12 year old:

(i) ≤15 kg 30mg BD x 5 days

(ii) >15 - 23 kg 45mg BD x 5 days

(iii) >23 - 40kg 60mg BD x 5 days

(iv) >40 kg 75mg BD x 5 days

5.3. Weight-based dosing of oseltamivir is recommended for infants <1 year of age. The AAP Committee on Infectious Diseases recommends oseltamivir 3 mg/kg per dose twice daily for full-term infants 0 through 8 months of age, and 3.5 mg/kg per dose

twice daily for full-term infants 9 through 11 months of age.Serious or life-threatening adverse effects associated with oseltamivir treatment were rare (<1%). However, gastrointestinal side effects including nausea and vomiting are common. These side effects are transient and usually resolve spontaneously within one to two days; and might be less severe when the drug is taken with food.

5.4. Minor neurological side effects like headache, insomnia or vertigo have been associated with treatment and prophylaxis of oseltamivir.

5.5. Vomiting was the only adverse effect reported to be more common than placebo in studies involving children aged 1-12 in adverse event data collected systemically in prospective trials. In addition, following reports from Japan of oseltamivir-attributable neuropsychiatric adverse effects, a review of controlled clinical trial data and ongoing surveillance has failed to establish a link between this drug and neurologic or psychiatric events.

6. Key References

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