Antiviral Drugs for Seasonal Influenza 2017-2018 ................................................................. p 1
Antiviral Drugs for Seasonal Influenza 2017-2018

Antiviral drugs can be used for treatment and prophylaxis of influenza. Frequently updated information on influenza activity, testing for influenza, and antiviral resistance is available from the CDC at www.cdc.gov/flu.

RECOMMENDATIONS FOR TREATMENT — The CDC recommends starting antiviral treatment as soon as possible after illness onset, without waiting for the results of influenza testing.

Antiviral treatment is recommended for all persons with suspected or confirmed influenza who have severe, complicated, or progressive illness, require hospitalization, or are at higher risk for complications, including children <5 years old (especially those <2 years old), persons <19 years old receiving long-term aspirin therapy, adults ≥65 years old, morbidly obese persons (BMI ≥40), women who are pregnant or ≤2 weeks postpartum, persons of American Indian/Alaska Native heritage, residents of nursing homes or other chronic care facilities, and persons who are immunosuppressed or have certain chronic medical conditions (including pulmonary, cardiovascular, renal, hepatic, hematological, metabolic, neurologic, or neurodevelopmental disorders).

Antiviral treatment can be considered for previously healthy persons with suspected or confirmed influenza if it can be started within 48 hours of illness onset.1,2

RECOMMENDATIONS FOR CHEMOPROPHYLAXIS — Antiviral prophylaxis is not recommended for healthy persons exposed to influenza. It can be considered after exposure for persons at high risk for complications who cannot receive the influenza vaccine or received it within the last 2 weeks, and for those who are unlikely to respond to vaccination. Prophylaxis is recommended to help control confirmed influenza outbreaks in nursing homes; antiviral medication should be given to residents and to unvaccinated healthcare workers.

DRUGS OF CHOICE — Neuraminidase inhibitors remain the drugs of choice for treatment and prophylaxis of influenza. They are active against both influenza A and B viruses. Oral oseltamivir (Tamiflu, and generics) and inhaled zanamivir (Relenza) are FDA-approved for treatment and prophylaxis of influenza. IV peramivir (Rapivab) is FDA-approved only for treatment of influenza.3

Use of amantadine or rimantadine is not recommended because of high levels of resistance to these drugs among currently circulating influenza A viruses; they are not active against influenza B viruses.

EFFECTIVENESS — Use of neuraminidase inhibitors for treatment of uncomplicated influenza shortens the duration of symptoms by about one day in adults.4,5 A meta-analysis of randomized trials in children with influenza found that treatment with oseltamivir within 48 hours of symptom onset reduced illness duration by about 18 hours overall (by 30 hours when trials that enrolled only children with asthma were excluded from the analysis) and lowered the risk of developing otitis media.6 Although most controlled trials of these drugs have not been powered to assess their efficacy in preventing serious influenza complications, experts have generally interpreted the combined results of controlled trials, observational studies, and meta-analyses as showing that early antiviral treatment of high-risk patients with influenza may reduce the risk of complications.7,8

When used for prophylaxis against susceptible strains of seasonal influenza A or B viruses, neuraminidase inhibitors have generally been about 70-90% effective.9
TIMING AND DURATION — Treatment of influenza with a neuraminidase inhibitor is most effective when started within 48 hours of illness onset; however, the results of some observational studies in hospitalized and critically ill patients suggest that treatment started as late as 4-5 days after illness onset may reduce the risk of complications such as pneumonia, respiratory failure, and death.10-12

The usual duration of treatment for patients with uncomplicated influenza is 5 days with oseltamivir or zanamivir and 1 day with peramivir. Oseltamivir is recommended for hospitalized, critically ill, or immunocompromised patients, in whom viral replication may be protracted; in such patients, a longer treatment course (e.g., 10 days) is often used. Peramivir (for at least 5 days) may be considered for those who cannot take oseltamivir.1

When indicated, prophylaxis with oseltamivir or zanamivir should be started within 48 hours after exposure to the influenza virus and continued for 7 days after the last known exposure. Longer durations of prophylaxis are often recommended for institutional and community outbreaks (see Table 1).

PREGNANCY — Pregnant women are at increased risk for severe complications of influenza, including death.13 Oseltamivir and zanamivir appear to be safe for use during pregnancy.14 Prompt treatment, preferably

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Table 1. Antiviral Drugs for Seasonal Influenza 2017-2018

<table>
<thead>
<tr>
<th>Drug</th>
<th>Oseltamivir (Tamiflu)</th>
<th>Zanamivir (Relenza)</th>
<th>Peramivir (Rapivab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulations</td>
<td>30, 45, 75 mg caps2; 6 mg/mL oral susp</td>
<td>5 mg/blister for inhalation2</td>
<td>200 mg/20 mL single-use vials</td>
</tr>
<tr>
<td>Cost</td>
<td>generic: $96.60</td>
<td>Tamiflu: $151.90</td>
<td>$950.00</td>
</tr>
<tr>
<td>Treatment of Uncomplicated Influenza</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult Dosage</td>
<td>75 mg PO bid x 5 days3</td>
<td>2 inhalations bid x 5 days</td>
<td>600 mg IV once4</td>
</tr>
<tr>
<td>Pediatric Dosage</td>
<td>30-75 mg PO bid x 5 days4</td>
<td>≥7 yrs: 2 inhalations bid x 5 days</td>
<td>2-12 yrs: 12 mg/kg (max 600 mg) IV once4</td>
</tr>
</tbody>
</table>

Dosage for Renal Impairment

- Adults: CrCl 10-30 mL/min: 30 mg once/d HD: 30 mg after every HD6 CAPD: 30 mg after exchange ESRD not on HD: no recommended
- No dosage adjustment required for renal impairment
- 2-12 yrs: CrCl 30-49 mL/min: 4 mg/kg once CrCl 10-29 mL/min: 2 mg/kg once ≥13 yrs: CrCl 30-49 mL/min: 200 mg once CrCl 10-29 mL/min: 100 mg once HD: administer dose (based on CrCl) after HD

Prophylaxis of Influenza

- Adult Dosage: 75 mg PO once/d x 7 days5,10 2 inhalations once/d x 7 days5,10 Not FDA-approved for prophylaxis
- Pediatric Dosage: 30-75 mg PO once/d x 7 days6,10 ≥5 yrs: 2 inhalations once/d x 7 days5,10 Not FDA-approved for prophylaxis

Dosage for Renal Impairment

- Adults: CrCl 10-30 mL/min: 30 mg once/d CrCl ≥30 mL/min: 30 mg every other day HD: 30 mg after every other HD11 CAPD: 30 mg once/week after exchange ESRD not on HD: no recommended
- No dosage adjustment required for renal impairment Not FDA-approved for prophylaxis
with oseltamivir, is recommended for women with suspected or confirmed influenza who are pregnant or ≤2 weeks postpartum.\textsuperscript{15-17} Antiviral prophylaxis can be considered for pregnant women who have had close contact with someone likely to have been infected with influenza. Zanamivir may be preferred for prophylaxis because of its limited systemic absorption, but oseltamivir is a reasonable alternative, especially for women at increased risk for respiratory problems.

**RESISTANCE** — Nearly all (>99%) of the recently circulating influenza virus strains tested by World Health Organization (WHO) Collaborating Centres around the world, including the CDC, have been susceptible to neuraminidase inhibitors.\textsuperscript{18} Resistance of some virus strains (particularly influenza A [H1N1]) to oseltamivir or peramivir can emerge during or after treatment, especially in immunocompromised patients with prolonged viral shedding.\textsuperscript{19,20} Resistant isolates have generally remained susceptible to zanamivir, but reduced susceptibility to zanamivir has been reported.\textsuperscript{21,22}

**ADVERSE EFFECTS** — Nausea, vomiting, and headache are the most common adverse effects of oseltamivir; taking the drug with food may minimize GI adverse effects. Diarrhea, nausea, sinusitis, fever, and arthralgia have been reported with zanamivir. Inhalation of zanamivir can cause bronchospasm; the drug should not be used in patients with underlying airway disease. Diarrhea and neutropenia have occurred with peramivir.

Neuropsychiatric events, including self-injury and delirium, have been reported in patients taking neuraminidase inhibitors, but a cause-and-effect relationship has not been established, and neuropsychiatric dysfunction is a known complication of influenza illness itself.\textsuperscript{23}

**DRUG INTERACTIONS** — Neuraminidase inhibitors administered within 48 hours before or ≤2 weeks after administration of the intranasal live-attenuated influenza vaccine (FluMist Quadrivalent) may interfere with the vaccine's efficacy. The live-attenuated vaccine is not recommended for use during the 2017-2018 influenza season because it has been less effective than the inactivated vaccine in recent seasons.\textsuperscript{24} Inactivated influenza vaccine can be given at any time relative to use of a neuraminidase inhibitor. ■
