<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dosage &amp; Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relenza® (zanamivir)</td>
<td>Treatment of influenza in patients aged 7 years and older who have been</td>
<td>Treatment of influenza:</td>
</tr>
<tr>
<td>oral inhalation powder</td>
<td>symptomatic for no more than 2 days.</td>
<td>• 10 mg twice daily for 5 days</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis of influenza in patients aged 5 years and older.</td>
<td>Prophylaxis of influenza:</td>
</tr>
<tr>
<td></td>
<td>Important limitations on use of zanamivir:</td>
<td>• Household setting: 10 mg once daily for 10 days</td>
</tr>
<tr>
<td></td>
<td>• Not recommended for treatment or prophylaxis of influenza in:</td>
<td>• Community Outbreak: 10 mg once daily for 28 days</td>
</tr>
<tr>
<td></td>
<td>• Individuals with underlying airways disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Not proven effective for:</td>
<td></td>
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<tr>
<td></td>
<td>• Treatment in individuals with underlying airways disease.</td>
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<tr>
<td></td>
<td>• Prophylaxis in nursing home residents.</td>
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<tr>
<td></td>
<td>The 10-mg dose is provided by 2 inhalations (one 5-mg blister per</td>
<td></td>
</tr>
<tr>
<td></td>
<td>inhalation).</td>
<td></td>
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<tr>
<td>Agent</td>
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<tr>
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</tbody>
</table>
| **Tamiflu® (oseltamivir) capsules**, oral suspension | Treatment of acute, uncomplicated influenza in patients 2 weeks of age and older who have been symptomatic for no more than 2 days. | Treatment of influenza:  
- Adults and adolescents (13 years and older): 75 mg twice daily for 5 days  
- Pediatric patients 1 to 12 years of age: Based on weight twice daily for 5 days  
- Pediatric patients 2 weeks to less than 1 year of age: 3mg/kg twice daily for 5 days  
- Renally impaired adult patients (creatinine clearance >30-60 mL/min): Reduce to 30 mg twice daily for 5 days  
- Renally impaired adult patients (creatinine clearance >10-30 mL/min): Reduce to 30 mg once daily for 5 days  
- ESRD patients on hemodialysis: Reduce to 30 mg after every hemodialysis cycle. Treatment duration not to exceed 5 days  
- ESRD patients on CAPD: Reduce to a single 30 mg dose administered immediately after a dialysis exchange  

Prophylaxis of influenza:  
- Adults and adolescents (13 years and older): 75 mg once daily for at least 10 days - Community outbreak: 75 mg once daily for up to 6 weeks  
- Pediatric patients 1 to 12 years of age: Based on weight once daily for 10 days - Community outbreak: Based on weight once daily for up to 6 weeks  
- Renally impaired adult patients (creatinine clearance >30-60 mL/min): Reduce to 30 mg once daily  
- Renally impaired adult patients (creatinine clearance >10-30 mL/min): Reduce to 30 mg once every other day  
- ESRD patients on hemodialysis: Reduce to 30 mg after alternate hemodialysis cycles for the recommended duration of prophylaxis  
- ESRD patients on CAPD: Reduce to 30 mg once weekly immediately after dialysis exchange for the recommended duration of prophylaxis |

Important limitations of use:  
- Efficacy not established in patients who begin therapy after 48 hours of symptoms.  
- Not a substitute for annual influenza vaccination.  
- No evidence of efficacy for illness from agents other than influenza viruses types A and B.  
- Consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use.
CLINICAL RATIONALE
Guidelines
The Center for Disease Control and Prevention (CDC) does not recommend widespread or routine use of antiviral medications for chemoprophylaxis so as to limit the possibilities that antiviral resistant viruses could emerge. Indiscriminate use of chemoprophylaxis might promote resistance to antiviral medications, or reduce antiviral medication availability for treatment of persons at higher risk for influenza complications or those who are severely ill.
To be effective as chemoprophylaxis, an antiviral medication must be taken each day for the duration of potential exposure to a person with influenza and continued for 7 days after the last known exposure. For persons taking antiviral chemoprophylaxis after inactivated influenza vaccination, the recommended duration is until immunity after vaccination develops (antibody development after vaccination takes about two weeks in adults and can take longer in children depending on age and vaccination history).3

Efficacy
The efficacy of zanamivir in the treatment of influenza in adults and adolescents 12 years of age and older was studied in placebo-controlled trials which showed 1-1.5 days in median time to improved symptoms.1

The efficacy of zanamivir in the treatment of influenza in pediatric patients age 5-12 years of age was studied in a placebo-controlled trial. Median time to symptom improvement was 1 day shorter in subjects receiving zanamivir compared with placebo. Although this trial was designed to enroll children aged 5 to 12 years, the product is indicated only for children aged 7 years and older. This evaluation is based on the combination of lower estimates of treatment effect in 5- and 6-year-olds compared with the overall trial population, and evidence of inadequate inhalation through the Diskhaler in a pharmacokinetic trial.1

The efficacy of oseltamivir in preventing naturally occurring influenza illness has been demonstrated in 2 post-exposure prophylaxis trials in households and 2 seasonal prophylaxis trials during community outbreaks of influenza. For household prophylaxis, the incidence of symptomatic laboratory-confirmed influenza was reduced from 19.0% for the placebo group to 4.1% for the zanamivir group. For seasonal prophylaxis, one trial with mostly unvaccinated (86%) individuals, the incidence of symptomatic laboratory-confirmed influenza was reduced from 6.1% for the placebo group to 2.0% for the group receiving zanamivir. For seasonal prophylaxis where 67% of the patients were vaccinated, the incidence of symptomatic laboratory-confirmed influenza was reduced from 1.4% for the placebo group to 0.2% for the zanamivir group.1

The efficacy of oseltamivir in the treatment of influenza in geriatric adults ≥65 years of age, and adults and adolescents 13 years of age and over, was studied in placebo-controlled double blind clinical trials. There was a 1 day (geriatric) to 1.3 (adult and adolescents) day reduction in median time to improvement in influenza infected subjects receiving oseltamivir compared to placebo.2

The efficacy of oseltamivir in the treatment of influenza in pediatric patients 1-12 years of age was studied in one double-blind placebo-controlled study. Oseltamivir reduced the total composite time to freedom from illness by 1.5 days compared to placebo.2

Pediatric patients age 2 weeks to 1 years of age was studied with oseltamivir in two open label trials which evaluated safety and pharmacokinetics. Pharmacokinetic data indicated
that a dose of 3 mg/kg twice daily in pediatric subjects 2 weeks to less than 1 year of age provided oseltamivir concentrations similar to or higher than those observed in older pediatric patients and adults receiving the approved dose and, by extrapolation, is expected to provide similar efficacy.\(^2\)

For adults and adolescent (13 years of age and older) patients, the efficacy of oseltamivir in preventing naturally occurring influenza illness has been demonstrated in three seasonal prophylaxis studies and a postexposure prophylaxis study in households. Depending on the population and setting, oseltamivir reduced the incidence of laboratory confirmed clinical influenza to <1%-1% from 5%-12% for placebo.\(^2\)

For pediatric patients 1-12 years of age, the efficacy of oseltamivir in preventing naturally occurring influenza illness has been demonstrated in a randomized, open-label, postexposure prophylaxis study in households that included pediatric subjects aged 1 to 12 years, both as index cases and as family contacts. Oseltamivir reduced the incidence of laboratory-confirmed clinical influenza from 17% in the group not receiving prophylaxis to 3% in the group receiving prophylaxis.\(^2\)

The efficacy of oseltamivir for seasonal prophylaxis of influenza in immunocompromised subjects was studied in a double-blind placebo-controlled study. The incidence of confirmed clinical influenza was 3% in the group not receiving oseltamivir compared with 2% in the group receiving oseltamivir; this difference was not statistically significant. A secondary analysis was performed using the same clinical symptoms and reverse transcription polymerase chain reaction (RT-PCR) for laboratory confirmation of influenza infection. Among subjects who were not already shedding virus at baseline, the incidence of RT-PCR-confirmed clinical influenza infection was 3% in the group not receiving oseltamivir and <1% in the group receiving oseltamivir.\(^2\)

**Safety**

Zanamivir is contraindicated in patients with history of allergic reaction to any ingredient of Relenza, including milk proteins.\(^1\)

Oseltamivir is contraindicated in patients with known serious hypersensitivity to oseltamivir or any of the components of Tamiflu.\(^2\)

**REFERENCES**

Anti-Influenza Agent Quantity Limit

OBJECTIVE
The intent of the Anti-Influenza Agent Quantity Limit is to help encourage appropriate dosage according to FDA label and/or guidelines. The program accommodates for two rounds of influenza treatment or 20 days of prophylaxis in a 120 day period. Requests for larger quantities will be evaluated through the Clinical Review process when the prescriber provides evidence that dosing with higher quantities is appropriate for the patient.

PROGRAM QUANTITY LIMITS

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity per 120 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relenza (zanamivir)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 mg blister</td>
<td>12504080008020</td>
<td>M, N, O, or Y</td>
<td>40 blisters</td>
</tr>
<tr>
<td>Tamiflu (oseltamivir)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 mg capsule&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12504060200110</td>
<td>M, N, O, or Y</td>
<td>20 capsules</td>
</tr>
<tr>
<td>45 mg capsule&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12504060200115</td>
<td>M, N, O, or Y</td>
<td>20 capsules</td>
</tr>
<tr>
<td>75 mg capsule&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12504060200120</td>
<td>M, N, O, or Y</td>
<td>20 capsules</td>
</tr>
<tr>
<td>6 mg/ml suspension</td>
<td>12504060201910</td>
<td>M, N, O, or Y</td>
<td>360 ml</td>
</tr>
<tr>
<td>12 mg/ml suspension</td>
<td>12504060201920</td>
<td>M, N, O, or Y</td>
<td>150 ml</td>
</tr>
</tbody>
</table>

<sup>a</sup> – generic available

QUANTITY LIMIT AUTHORIZATION CRITERIA FOR APPROVAL
Requests above the set quantity limit will be approved when BOTH of the following are met:

1. ONE of the following:
   a. The patient requires additional courses of therapy due to additional episodes of acute influenza infection
      **OR**
   b. The patient requires additional courses or increased duration of therapy for prophylaxis after exposure to an influenza infected person

   **AND**

2. ONE of the following:
   a. BOTH of the following:
      i. The requested quantity (dose) is less than or equal to the FDA labeled dose
      **AND**
      ii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
      **OR**
   b. BOTH of the following:
      i. The requested quantity (dose) is greater than the FDA labeled dose
      **AND**
      ii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 4 months