IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

** Benefit determinations should be based in all cases on the applicable contract language. ** To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

** Description **

Oseltamivir (Tamiflu®) is an anti-viral medication (neuraminidase inhibitor) administered orally for the treatment or prevention of influenza. It should not be considered a substitute for annual influenza vaccination.

For the treatment of adults with influenza, the FDA-approved dose of oseltamivir is one capsule (75 mg) twice daily for five days (a total of 10 capsules per course).

For prevention of influenza in a household setting, the FDA-approved dose of oseltamivir is one capsule (75 mg) once daily for ten days (a total of 10 capsules per course).
Policy/Criteria

I. Most contracts require prior authorization approval of oseltamivir for coverage of quantities greater than 20 capsules (two, courses), or four 60-ml bottles of suspension (two, courses) every six months for the treatment of influenza. Oseltamivir in quantities up to 20 capsules or four 60-ml bottles of suspension every six months may be considered medically necessary and may be covered without prior authorization.

II. Oseltamivir in quantities up to 42 capsules, or nine 60-ml bottles of suspension (a six week course) every six months may be considered medically necessary for seasonal prophylaxis of influenza when both criteria A and B below are met.
   A. The current influenza vaccination is contraindicated or not effective against prevalent circulating strains.
   AND
   B. There is a high risk of complications from influenza (see Appendix 1 for high risk criteria).

III. Administration, Quantity Limitations and Authorization Period
   A. OmedaRx considers oseltamivir to be a self-administered medication.
   B. When policy criteria are met, oseltamivir may be authorized in quantities up to 42 capsules, or nine 60-ml bottles of suspension (a six week course) every six months. Quantities exceeding 42 capsules, or nine 60-ml bottles of suspension every six months are considered investigational.
   C. Authorization shall be reviewed every six months to confirm that medical necessity criteria are met and the medication is effective.

Position Summary
- Influenza vaccination is the primary method for preventing influenza and its severe complications particularly in individuals at high risk for influenza-related complications. [1]
- Oseltamivir is an oral neuraminidase inhibitor that has activity against influenza A and B virus. It has only been shown to be effective for the treatment of influenza if started within the first two days (48 hours) of symptom onset. [2-8]
- The demonstrated benefit with neuraminidase inhibitors (oseltamivir, zanamivir, and peramivir) is limited to a modest improvement in symptoms.
- One treatment course of oseltamivir every six months will provide coverage for the typical influenza season.
- The safety and effectiveness of concomitant administration of oseltamivir and zanamivir or oseltamivir and peramivir have not been established.
Background

- There is renewed interest in use of oseltamivir because of the high rates of resistance reported to amantadine and rimantadine (up to 92% of influenza A and B isolates). [8]
- Oseltamivir- and zanamivir-resistant strains of influenza A have also begun to emerge as use of these newer antiviral medications increases.
  - Approximately 10% of influenza A (H1N1) isolates were resistant to oseltamivir during the 2007 - 2008 influenza season. [8]
  - Because rates of resistance are relatively low, oseltamivir and zanamivir are still recommended by the CDC as preferred options for chemoprophylaxis in high-risk individuals after exposure to influenza. [8]
  - Immunization with influenza vaccine as a means to prevent influenza may help limit unnecessary exposure to oseltamivir and zanamivir, thereby slowing the spread of resistance.
- According to the CDC, influenza vaccination is the primary method for preventing influenza and its severe complications particularly in individuals at high risk for influenza-related complications. [8] High-risk patients are defined in Appendix 1.
- Oseltamivir does not have activity against bacterial infections. The FDA has received reports of patients with serious bacterial infections who initially had influenza-like symptoms and who had progressions of bacterial infection during treatment with anti-influenza drugs alone. [9]

Clinical Efficacy

Treatment of acute influenza:

- Treatment of influenza A or B with oseltamivir, zanamivir, or peramivir (neuraminidase inhibitors) decreases the duration of symptoms by about a day when compared with placebo. [2-3, 21]
- A Cochrane review noted that the quality of the data for neuraminidase inhibitors is extremely poor due to missing study details and the high likelihood of publication and reporting bias. They state that it is not possible to draw robust and unequivocal conclusions with regard to the efficacy of these products. [18]
- Treatment with oseltamivir provided no benefit in the time it took patients with influenza to return to normal activity levels. [18]
- The potential benefit versus risk with neuraminidase inhibitors has not been established in patients at high risk for complication from influenza.
- Concomitant administration of oseltamivir plus zanamivir has not been shown improve clinical outcomes such as resolution of influenza symptoms when compared with oseltamivir alone. [20]
Prevention of influenza (community outbreak):
- Oseltamivir was studied in 548 frail, elderly residents of residential and nursing homes for community outbreak prophylaxis. Patients were stratified by vaccination status and coexisting chronic obstructive pulmonary disease (COPD). [4]
  * Most patients had multiple concomitant diseases with a mean of six diseases per patient. There was a mean of 7.7 concomitant medications per patient.
  * Approximately 14% of the population had coexisting COPD. Approximately 80% of the patients were vaccinated before the influenza season.
  * Oseltamivir 75 mg orally once per day or placebo was initiated for six weeks when influenza was confirmed in the home or reported in the area.
  * Lab-confirmed influenza and influenza-like illness occurred in 12 of 272 (4.4%) patients receiving placebo versus 1 of 276 (0.4%) patients receiving oseltamivir.
  * The reported protective efficacy was 92 % (p = 0.002) for oseltamivir.
  * The absolute risk reduction (ARR) and number needed to treat (NNT) for oseltamivir were 4.0% and 25, respectively.
- There are no that directly compare the efficacy or effectiveness of oseltamivir (Tamiflu), zanamivir (Relenza), or peramivir (Rapivab) with influenza vaccine in the prevention of influenza.

Avian influenza ('bird flu') and H1N1 influenza ('swine flu'):
- There is no evidence for neuraminidase inhibitors (oseltamivir, zanamivir and peramivir) with regard to their efficacy in the treatment or prevention of avian influenza ('bird flu') or H1N1 flu ('swine flu'). Potential for efficacy is based on in vitro virological data and extrapolation from use in treating ordinary human influenza.
**Dosing and Administration**

- **Dosing of oseltamivir for treatment of influenza A and B:**
  
  * **Adults and adolescents (13 years and older):** 75 mg orally twice a day for five days. [2]
  
  * **Pediatric patients (2 weeks to 12 years of age):** [2]

<table>
<thead>
<tr>
<th>Weight</th>
<th>Recommended dose for 5 days</th>
<th>Number of 60 ml bottles needed for recommended dose</th>
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<tbody>
<tr>
<td>Patients from 2 weeks to &lt; 1 year of age</td>
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<td></td>
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<tr>
<td>Any weight</td>
<td>3 mg/kg twice daily</td>
<td>1</td>
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<tr>
<td>Patients from 1 year to 12 years of age based on body weight</td>
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<tr>
<td>≤ 33 lbs (≤ 15 kg)</td>
<td>30 mg (5 ml) twice daily</td>
<td>1</td>
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<tr>
<td>&gt; 33 lbs to 51 lbs (&gt; 15 kg to 23 kg)</td>
<td>45 mg (7.5 ml) twice daily</td>
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<tr>
<td>&gt; 51 lbs to 88 lbs (&gt; 23 kg to 40 kg)</td>
<td>60 mg (10 ml) twice daily</td>
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</tr>
<tr>
<td>&gt; 88 lbs (&gt; 40 kg)</td>
<td>75 mg (12.5 ml) twice daily</td>
<td>3</td>
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* **Renally impaired adolescent and adult patients (creatinine clearance < 60 ml/min):**
  
  Dose reduction is necessary and is based on creatinine clearance (degree of renal impairment). Refer to prescribing information for specific dose adjustments. [2]

- **Dosing of oseltamivir for prevention of influenza A and B:**

  * **Adults and adolescents (13 years and older):** 75 mg orally once daily for at least ten days. May use for up to 6 weeks for a community outbreak. [2]

  * **Pediatric patients (1 to 12 years of age):** [2]

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* **The safety and effectiveness of prophylaxis of influenza with oseltamivir have not been established in infants less than one year of age.**
* Renally impaired adult and adolescent patients (creatinine clearance < 60 ml/min):
Dose reduction is necessary and is based on creatinine clearance (degree of renal
impairment). Refer to prescribing information for specific dose adjustments. [2]

How supplied
- Oseltamivir is supplied as 30 mg, 45 mg, or 75 mg capsules or as a 6 mg/ml flavored
suspension available in 60 ml bottles. Once reconstituted, the suspension requires
refrigeration and is good for up to 17 days. [2]

Safety
- The most common adverse effects reported with oseltamivir administration include
nausea, vomiting, and diarrhea. [2]
- The number needed to harm for 1 patient to experience nausea or vomiting with
oseltamivir treatment over five days is 10 patients.
- Oseltamivir is classified as Pregnancy Category C and should be used during pregnancy
only if the potential benefit justifies the potential risk to the fetus based on the
physician’s medical judgment in consultation with the patient. [2]

Preventing the spread of influenza: [19]
- Influenza is thought to spread mainly by person-to-person through coughing or sneezing
of infected people.
  * Cover your nose and mouth with a tissue when you cough or sneeze. Throw the
tissue in the trash after you use it.
  * Wash your hands often with soap and water, especially after you cough or sneeze.
Alcohol-based hand cleaners are also effective.
  * Avoid touching your eyes, nose, or mouth. Germs spread that way.
  * Stay home if you get sick. The CDC recommends that you stay home from work
or school and limit contact with others to keep from infecting them.
1. Equal to or greater than 50 years old.
2. All children aged 6–59 months.
3. Residents of nursing homes and other chronic-care facilities with residents of any age who have chronic medical conditions.
4. Adults and children with underlying chronic medical conditions such as:
   a. Chronic pulmonary diseases (e.g., asthma or chronic airway obstructive disorders)
   b. Cardiovascular disease (except isolated hypertension)
   c. Endocrine (e.g. diabetes) and chronic metabolic disorders
   d. Kidney dysfunction and liver disorders
   e. Blood disorders (e.g., hemoglobinopathies)
   f. Immune system problems (e.g., HIV infection; immunosuppressed by medication, chemotherapy, or radiation therapy)
   g. Neurological or neuromuscular disorders (such as spinal cord injuries, neuromuscular disorders, cognitive dysfunction)
   h. Morbid obesity (BMI of 40 or greater)
5. Children and adolescents aged 6 months to 18 years on chronic aspirin therapy. These patients may be at risk for developing Reye’s syndrome after influenza infection.
6. All women who will be pregnant during the influenza season.
7. American Indians and Alaskan Natives.

Cross References
Relenza®, zanamivir, Medication Policy Manual, Policy No. 113

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References

1. CDC: http://www.cdc.gov/nip/flu-vac-supply/flu-qa-top.htm
