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Drug Class Scan

Month/Year of Review: January 2012
PDL Class: Antivirals: Influenza

Date of Last Review: September 2010
Source Document: PS Report

Current Preferred Agents:
Amantadine
Rimantidine*
Oseltamivir* (Tamiflu®)

*with quantity limit

Current Non-Preferred Agents:
Zanamivir (Relenza®)

Previous Conclusions and Recommendations:

1. Vaccination is the primary method of preventing influenza infection.
2. The CDC currently does not recommend the use of amantadine or rimantadine for the treatment or prophylaxis of influenza A due to viral resistance.
3. The CDC recommends treatment of 2009 influenza A (H1N1) in 'at risk' adults and children with either oseltamivir or zanamivir.
4. Zanamivir uses a complex administration device for inhalation and should not be used in patients with pre-existing respiratory disorders.
5. Recommend taking into account current public health recommendations for appropriate populations, duration and dosing schedules.

PA Criteria/QL:
For treatment: Patient must have an OHP covered ICD9 diagnosis AND the antiviral is for the treatment of influenza
For prophylaxis: Patient must have an OHP covered ICD9 diagnosis AND be considered at high risk for complications for influenza
Quantity Limit: Oseltamivir requires PA for therapy exceeding five days

Methods:

Search Strategy
An Ovid MEDLINE search was conducted using the following search terms:
Influenza, human influenza, influenza A virus, influenza B virus, H1N1 subtype influenza A virus, flu, H5N1 subtype influenza A virus; antiviral, antiviral$, antiviral agents; RCT, randomized control trial, randomized control trials, trial$, clinical trial, controlled trial
The search was limited to studies conducted with humans in English language publications from 2008 to present.

Results:
The MEDLINE search retrieved 139 full citations. After a full review of citations and abstracts, no new head-to- or placebo-controlled RCTs using FDA approved agents were identified. Most of the RCTs identified compared oseltamivir with either neuraminidase inhibitors not approved for use in the US, or herbal/naturopathic agents. Many RCTs were related to vaccination. This search produced numerous articles analyzing the 2009 h1N1 pandemic; prevention and treatment were examined in various formats: articles, case studies, reviews, observational studies.

The search of the Cochrane website identified two new proposed protocols in regards to influenza: one to review treatment interventions (proposed 11/2010) and the other to review prevention interventions (5/2010). The current Cochrane review for treatment with neuraminidase inhibitors (last updated 2010) was not included due to lack of quality RCTs. Prior recommendation of oseltamivir over zanamivir has been removed pending more data; a new protocol for review was proposed 6/2011.
The search of the AHRQ, DERP, and VA/DoD websites did not identify any relevant systematic reviews. The search on the FDA websites identified no new approved drugs, no new indications, and one new safety alert.

New FDA-approved drugs:
None identified.

New FDA Indications:
None identified.

New FDA safety alerts:

Medication	Alert Date	FDA Alert
Oseltamivir (Tamiflu®) suspension	July 2011	**Warnings and Precautions:** **ISSUE:** Labeling changes are being made to Tamiflu oral suspension to reduce the possibility of prescribing and dosing confusion that can lead to medication errors. The changes to the product label include: • A change in the concentration of Tamiflu from 12 mg/mL to 6 mg/mL. The lower concentration of Tamiflu is less likely to become frothy when shaken, which helps to ensure an accurate measurement. A change in the measurements of the oral dosing

device from milligrams (mg = weight) to milliliters (mL = volume).
- A change in the dosing table for Tamiflu to include a column for the volume (mL) based on the new 6 mg/mL concentration. Revised container labels and carton packaging. Revised compounding instructions for pharmacies to prepare a 6 mg/mL oral suspension from Tamiflu capsules in an emergency situation only if the commercially manufactured Tamiflu for oral suspension is unavailable.

BACKGROUND: Tamiflu is in a class of medications called neuraminidase inhibitors. These drugs work by stopping the spread of the influenza (flu) virus in the body. Genentech, the manufacturer of Tamiflu for oral suspension, plans to begin distribution of the new 6 mg/mL product in July 2011. The company has instituted a voluntary Take Back Program for wholesale buyers, distributors and pharmacies to remove the 12 mg/mL product from the marketplace. The 12 mg/mL product will remain in the marketplace and in state or national stockpiles until current supplies expire.

RECOMMENDATION: It is important for healthcare professionals to be aware that a patient may potentially receive either concentration (6 mg/mL or 12 mg/mL) from their pharmacy during the next influenza season (2011-2012). Steps should be taken to avoid the potential for a medication error due to confusion between the two concentrations. Prescribers should include the new concentration (6 mg/mL) and dose in milliliters on all prescriptions for Tamiflu for oral suspension.

New Systematic Reviews:
None identified.

Guidelines[1]:

Centers for Disease Control and Prevention: Antiviral agents for the treatment and chemoprophylaxis of influenza[1].

- Antiviral treatment is recommended as soon as possible for patients with confirmed or suspected influenza who have severe, complicated, or progressive illness or who require hospitalization.
- Antiviral treatment is recommended as soon as possible for outpatients with confirmed or suspected influenza who are at higher risk for influenza complications on the basis of their age or underlying medical conditions; clinical judgment should be an important component of outpatient treatment decisions.
- Recommended antiviral medications include oseltamivir and zanamivir, on the basis of recent viral surveillance and resistance data indicating that >99% of currently circulating influenza virus strains are sensitive to these medications. Amantadine and rimantadine should not be used because of the high levels of resistance to these drugs among circulating influenza A viruses, but information about these drugs is provided for use if current recommendations change because of the reemergence of adamantane-susceptible strains.

- Oseltamivir may be used for treatment or chemoprophylaxis of influenza among infants aged <1 year when indicated.
- Antiviral treatment also may be considered on the basis of clinical judgment for any outpatient with confirmed or suspected influenza who does not have known risk factors for severe illness if treatment can be initiated within 48 hours of illness onset.

Duration of Treatment or Chemoprophylaxis[1]

Treatment: Recommended duration for antiviral treatment is 5 days. Longer treatment courses for patients who remain severely ill after 5 days of treatment can be considered.

Recommended duration is 7 days after exposure.

Chemoprophylaxis: For control of outbreaks in long-term care facilities (e.g. elderly nursing homes) and hospitals**,** CDC recommends antiviral chemoprophylaxis for a minimum of 2 weeks, and continuing up to 1 week after the last known case was identified. Antiviral chemoprophylaxis should be considered, especially for elderly long-term care facilities, for all exposed residents, including those who have received influenza vaccination.

References:

1. Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM, Centers for Disease Control and Prevention (CDC). Antiviral agents for the treatment and chemoprophylaxis of influenza --- recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Surveill Summ 2011 Jan 21;60(1):1-24

Appendix A: PA Criteria

Antivirals - Influenza

Goal(s): To ensure appropriate extended influenza drug use by authorizing utilization in specified patient population.

Length of Authorization: Date of service

Preferred Alternatives: See PDL options at : http://www.oregon.gov/DHS/healthplan/tools_prov/pdl.shtml

Requires PA:

Name of Drug	Brand	Quantity Limits
Zanamivir	Relenza	NA
Oseltamivir	Tamiflu	>5 days therapy requires a PA
Amantadine		NA

Approval Criteria		
1. What is the diagnosis being treated?	Record ICD9 code	
2. Is this an OHP covered diagnosis?	**Yes:** Go to #3	**No**: Pass to RPh, DENY (Not covered by the OHP)
3. Is the anitiviral being used to **treat** influenza?	**Yes:** Go to #4.	**No:** Go to #5
4. Will the prescriber consider a change to a preferred product? Message: • Preferred products do not require a PA. • Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Health Resource Commission (HRC). Reports are available at: http://www.oregon.gov/OHPPR/HRC/Evidence_Based_Reports.shtml.	**Yes:** Inform provider of covered alternatives in class. http://www.oregon.gov/DHS/healthplan/tools_prov/dl.shtml. Current recommended treatment duration*: - 5 days for the following: Relenza, Tamiflu, - Amantadine: Continue for at least 10 days.	**No**: Approve for 5 days
5. Does the patient have any of the following putting them at increased risk for complications requiring prophylaxis?	**Yes:** Approve for duration of prophylaxis.	**No:** Pass to RPh; Deny, (Not Medically Appropriate)

- High-risk persons during 2 weeks after vaccination before adequate immunity develops - Patients >1 years of age at high risk for complications for whom the vaccine is contraindicated, unavailable or expected to have low effectiveness - Residents in institutions such as nursing homes or long-term care facilities that are experiencing an influenza outbreak - Persons at high-risk of complications of influenza, such as transplant and immunocompromised patients	Current recommended duration of prophylaxis*; Relenza: 10 days for prophylaxis in a household setting, up to 28 days in a community outbreak setting. Tamiflu: at least 10 days following close contact with an infected individual; up to 6 weeks in a community outbreak setting. Amantadine: Up to 4 weeks.	