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Drug Utilization Review for Oklahoma Medicaid

Influenza Prevention and Treatment Strategies

Background and Epidemiology

Influenza is a major cause of missed school and workdays each year, and is responsible for hospitalizations and death resulting from complications of the infection. Each year, approximately 20,000 deaths nationwide are attributable to influenza, primarily in elderly persons and patients with co-morbidities that place them at high risk for these complications. While there is no cure for influenza, there are several strategies for the prevention and treatment of the infection.

Vaccination

The influenza virus vaccine has been widely available for several years and remains the gold standard for prevention of infection. The CDC Advisory Committee on Immunization Practices (ACIP) has updated its recommendations for target groups who should receive the vaccine for prevention. (Table 1)

The influenza vaccine is 70-90% effective in preventing influenza in healthy persons under age 65 when the yearly vaccine matches well with the circulating virus. In the elderly, young children, and high-risk populations, the vaccine may be only 30-60% effective in preventing influenza. While the influenza vaccine may not completely prevent influenza in this population, it can reduce the severity of the infection and help prevent complications, hospitalizations and deaths.

The influenza season generally runs from December through March in the United States. Because



it takes from two to four weeks for antibodies to form once the vaccine is given, the optimal time to immunize those in high-risk groups is from early October through mid-November, although the vaccination may be given at any time throughout the influenza season.

Other Forms of Treatment and Prevention

In the United States, there are currently four antiviral medications available for treatment and/or prevention of influenza. These medications are important as

adjunctive therapy to the vaccine or when the vaccine is contraindicated, but are not intended to be replacements for the vaccine.

The traditional antivirals, amantadine and rimantadine, inhibit early replication of the influenza virus by blocking an ion channel on the viral membrane. Both agents are effective for prophylaxis and treatment of influenza virus type A only. The neuraminidase inhibitors (NI) zanamivir and oseltamivir decrease the spread of influenza by preventing the release of viral particles from infected cells. These medications are effective against influenza type A and B. (Table 2)

Amantadine (Symmetrel), is indicated for the prophylaxis and treatment of influenza type A virus in adults and children one year and older. It was the first of the antiviral medications, having been available since 1966. Amantadine has been shown to be effective in both prevention and treatment of influenza type A.

For prevention of influenza, amantadine is about as effective as the vaccine when given throughout the

Table 1. Targeted Groups for Vaccination:

- * Persons 50 years and older
- * Residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions
- * Adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma
- * Adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by HIV)
- * Children and teens (six months to 18 years old) who are receiving long-term aspirin therapy and therefore might be at risk for developing Reye's syndrome after influenza infection
- * Women who will be in the second or third trimester of pregnancy during the influenza season (pregnant women who have medical conditions that increase their risk for complications from influenza should be vaccinated before the influenza season, regardless of the stage of pregnancy)

Additionally, the following groups should also be vaccinated to prevent spread of the virus:

- * Physicians, nurses and other personnel in hospital and outpatient-care settings, including emergency response workers
- * Employees of nursing homes, chronic-care facilities, assisted living and other residencies with persons in high-risk groups
- * Persons who provide home care to persons in high-risk groups
- * Household members (including children) of persons in high-risk groups

period of exposure. In determining the duration of treatment, cost, compliance and potential adverse effects should be considered, although dosing should continue for at least 10 days following a known exposure.

For treatment, amantadine has been shown to reduce the duration of illness by approximately one day if treatment is started early, preferably within the first 24-48 hours of onset of symptoms. Treatment should be continued for 24-48 hours after the disappearance of symptoms.

Adverse effects are mainly CNS related, with insomnia, anxiety, dizziness and depression occurring in up to one-third of patients. Amantadine requires dosing adjustments for patients with renal impairment, liver dysfunction, and in those 65 years and older. Amantadine has also been reported to increase the risk of seizures, and is contraindicated in individuals with seizure disorders.

Rimantadine (Flumadine), is indicated for influenza prophylaxis in adults and children one year and older and for treatment in patients 14 years and older. It became available in 1993, and, like amantadine, is effective only against influenza type A.

While rimantadine is as effective as amantadine for prophylaxis and treatment of influenza type A, rimantadine

is associated with fewer adverse effects. The most common adverse effects are nausea, vomiting and dyspepsia.

Rimantadine also requires dosing adjustments in elderly patients, those with liver dysfunction, and those with severe renal impairment.

The duration of therapy for prophylaxis is similar to that of amantadine; for treatment of influenza, rimantadine should be continued for approximately five to seven days from the onset of symptoms.

Zanamivir (Relenza) is one of the newest antivirals indicated for treatment of influenza type A and B in adults and children seven years and older. It is available as a powder for inhalation. Treatment should begin within 24-48 hours of onset of symptoms and continue for five days.

Zanamivir is associated with few minor adverse effects such as cough, sore throat, ear, nose and throat infections, and bronchitis. However, bronchospasm and decline in lung function have been reported in some patients, so it is not recommended in patients with chronic respiratory disease.

The use of zanamivir has resulted in a decrease in the average duration of influenza symptoms by one day.

Oseltamivir (Tamiflu) is indicated for treatment of influenza type A and B in adults and children one year and older, and for prevention in adults and adolescents 13 years and older. Oseltamivir is available in a capsule and liquid suspension.

Treatment should begin within 24-48 hours of the onset of symptoms and continue for five days.

For prophylaxis, the duration of therapy is dependent on the type of exposure. For community outbreaks of influenza, oseltamivir is dosed once daily and has been given safely to patients for up to six weeks. For exposure due to close contact with an infected person, oseltamivir is given two times daily for seven days. Dosage adjustments are necessary for renally impaired patients.

Nausea and vomiting are the most frequently reported adverse effects and are usually mild.

Oseltamivir has been shown to reduce the duration of influenza symptoms by an average of one to two days. Prophylaxis studies show that oseltamivir can reduce the

incidence of influenza in unvaccinated adults from 4.8% to 1.2%. In institutionalized, vaccinated patients, the incidence of influenza was reduced from 4.4% to 0.4%, and in households with an infected member, the incidence was reduced from 12% to 1%.

Summary

Newer, more tolerable antiviral medications have expanded the arsenal in the fight against influenza. However, the influenza vaccine remains the most cost-effective preventative therapy. One CDC "Healthy People 2010" goal is to achieve vaccination coverage for 90% of patients 65 years and older.

There is a high priority for expanding vaccine use in the high-risk group under age 65 as well as increasing vaccination of health-care workers. These measures should lead to a large reduction in hospitalizations, complications and deaths due to influenza.

Table 2. Comparison of Antivirals

Drug	Symmetrel (amantadine)	Flumadine (rimantadine)	Relenza (zanamivir)	Tamiflu (oseltamivir)
Indications/Age	Treatment: ≥ 1 yr Prophylaxis: ≥ 1 yr	Treatment: ≥ 14 yrs Prophylaxis: ≥ 1 yr	Treatment: ≥ 7 yrs Prophylaxis: N/A	Treatment: ≥ 1 yr Prophylaxis: ≥ 13yrs
Dose	For Treatment & Prophylaxis: Adult: 200 mg QD Child 9-12 yrs: 100 mg BID Child 1-9 yrs: 4.4-8.8 mg/kg/day, NTE 150mg/day	Treatment: Adult (≥ 14 yrs) 100 mg BID Prophylaxis: Adult: 100 mg BID Child <10 yrs: 5 mg/kg/day, NTE 150 mg/day	Treatment: ≥ 7 yrs: 10 mg (2 blisters) BID	Treatment: ≥ 13 yrs: 75mg BID Children: to 15kg: 30mg BID 15-23: 45mg BID >23-40: 60mg BID >40kg: 75mg BID Prophylaxis, Community outbreak ≥13 yrs: 75mg BID Prophylaxis, close contact: 75mg QD
Dosage Forms	Tablets, capsules, syrup	Tablets, syrup	Oral Inhaler	Capsule, suspension
AWP (5 day treatment)	\$3.66 (generic)	\$28.52	\$46.18	\$59.54

Utilization of Influenza Medications Oklahoma Medicaid 1999-2000

	Vaccine*	Flumadine/ Amantadine	Neuraminidase Inhibitors
# of patients	1578	2175	1028
Total \$	\$37,750	\$46,376	\$49,463
*Both pharmacy and medical claims			

- * Prescriptions per patient: Between September 1999 and February 2000, a total of 1,028 Medicaid recipients received at least one prescription for Relenza and/or Tamiflu. Twenty-two (2%) of these received more than one prescription.
- * Units per prescription: The majority of prescriptions were filled for a quantity equal to five days of therapy
- * Additional use of other therapies: Of the 1,028 recipients using an NI, 17 also used an older flu medication (Symmetrel or Flumadine).
- * Use of flu vaccination: For this time period, 1,578 Medicaid recipients had a paid claim for a flu vaccination. Of this group, five went on to receive a prescription for a neuraminidase inhibitor. Eleven received an older flu medication.

Update on Rx-POS and Pro-DUR Upgrade

As described in the previous issue of the OkDUR Newsletter, the Oklahoma Health Care Authority and Unisys are working toward the implementation of a new prescription point-of-sale (Rx-POS) and prospective Drug Utilization Review (pro-DUR) system. The testing phase is almost complete, and the anticipated implementation date is late March.

The first pro-DUR module to be turned on will identify early prescription refills. Specifically, an early refill alert will be generated if less than 75% of the previous fill has been exhausted or if the refill is seven or more days early. An "early refill" alert will result in a rejection of that pharmacy claim.

Subsequent modules to be implemented will include high dose, therapeutic duplication, drug-drug interaction, ingredient duplication, and drug-pregnancy/lactation interactions. Some alerts will result in an educational alert to the pharmacist, others will result in a rejected pharmacy claim.

Refer to the Fall OkDUR Newsletter for specifics on this new program. Also, the Medicaid pharmacy helpdesk will be available to assist with questions and issues as they arise.

Medicaid Pharmacy Help Desk Contact Numbers

- 271-6349 (Pharmacist OKC metro)
- 1-800-831-8921 (Pharmacist toll free)
- 271-9048 (Prescriber OKC metro)
- 1-877-269-2768 (Prescriber toll free)

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