



September 2015 Issue

## From the Front Lines

AlixaRx Clinical Pharmacists Address Everyday Challenges in Long-Term Care

### Zyvox (linezolid)

Zyvox (linezolid) is an antibiotic effective against a wide spectrum of gram-positive organisms, including resistant strains such as methicillin-resistant staphylococcus (MRSA) and vancomycin-resistant enterococci (VRE). It is often the topic of pharmacy recommendations due to the potential of serious side effects, drug interactions, inappropriate use and cost.

#### Antibiotic Stewardship and Appropriate Use

Antibiotic stewardship is the term used to describe the process of selecting the optimal antibiotic medication, dose, duration of therapy, and route of administration.<sup>1</sup> It requires that the most appropriate antibiotic be used in any given situation. Antibiotic stewardship decreases the likelihood of developing resistant organisms, maximizes cost effectiveness, and improves patient outcomes.

When applying the concept of antibiotic stewardship to Zyvox, we first need culture and sensitivity (C&S) results showing susceptibility to Zyvox. It is important to note that Zyvox is usually not appropriate for empiric therapy. Once susceptibility has been determined by C&S, Zyvox may be an appropriate antibiotic for treating a patient's infection. Here are some examples of situations where Zyvox may be appropriate:

- The patient's culture and sensitivity shows susceptibility to IV vancomycin and to Zyvox, but the patient is unable to tolerate IV vancomycin.
- The patient's culture and sensitivity shows susceptibility to IV vancomycin and to Zyvox, but the IV access cannot be established.
- The patient's culture and sensitivity shows vancomycin-resistant enterococcus (VRE) susceptible for Zyvox.

The following chart shows the indications for use of Zyvox in adult patients, along with the recommended dose and length of therapy. Courses of treatment longer than 28 days are not typical and increase the risk for additional side effects like lactic acidosis, peripheral neuropathy and optic neuropathy.<sup>2</sup>

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Indication	Dose	Length of Therapy
Nosocomial pneumonia caused by Staph. aureus or MRSA	600 mg IV or PO Q12 hours	10-14 days
Community-acquired pneumonia caused by Strep. pneumoniae or Staph. aureus	600 mg IV or PO Q12 hours	10-14 days
Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, caused by Staph. aureus, MRSA, or Strep. agalactiae	600 mg IV or PO Q12 hours	10-14 days
Uncomplicated skin and skin structure infections caused by Staph. aureus or Strep. pyogenes	400 mg PO Q12 hours	10-14 days
Vancomycin-resistant Enterococcus faecium (VRE) infections	600 mg IV or PO Q12 hours	14-28 days

### Alternatives to Zyvox

Alternatives to Zyvox for treatment of MRSA may include IV vancomycin, daptomycin (Cubicin), and tigacycline (Tygacil), depending on the site of infection and the culture and sensitivity. IV vancomycin is by far the most cost-effective option, as Zyvox costs more than 10 times more than vancomycin. Zyvox is the only medication of this group to offer a PO route of administration (tablets and oral suspension).

### Side Effects

Zyvox, like many antibiotics, can cause diarrhea, headache, nausea, and vomiting. However, when nausea and vomiting occurs with Zyvox, it may indicate lactic acidosis. Zyvox can also cause myelosuppression, including anemia, leukopenia, pancytopenia, and thrombocytopenia. Optic neuropathy is also a possible side effect, especially when Zyvox is used for longer than 28 days.

### Serotonin Syndrome

Serotonin syndrome is a condition caused by excess serotonin in the body. It is the most significant drug-drug interaction involving Zyvox. Signs and symptoms of serotonin syndrome may include stiff muscles, confusion, racing heartbeat, diarrhea, nausea, vomiting, high fever, shivering, hallucinations, very high or very low blood pressure, large pupils or sweating.

### Monitoring

Labs: Complete blood count (CBC) weekly, due to the risk of myelosuppression. This is particularly important in patients who already have myelosuppression or who have a history of myelosuppression.

Nursing: Nurses should monitor the patient's blood pressure, heart rate, and temperature daily and monitor for the signs and symptoms of serotonin syndrome and other side effects.

### Pharmacy Recommendations

AlixRx Clinical Pharmacists will issue a recommendation to the provider when Zyvox is ordered for a patient on a medication that may increase the risk of serotonin syndrome. Many of these medications are antidepressants. A more detailed list of these medications can be found at the end of this article.<sup>3</sup> Recommendations may request that an alternative antibiotic be considered, that an interacting drug be held until Zyvox is completed, or that CBC or other lab monitoring be initiated.

The drug interactions and side effects of Zyvox are important to watch out for, but equally important is its place in treating MRSA and VRE infections. With proper antibiotic stewardship, patient monitoring, and a clear understanding the risks and benefits of Zyvox, we can help our patients recover as quickly as possible.

**I. Serotonergic psychiatric drugs implicated in the AERS cases of serotonin syndrome with linezolid**

Selective Serotonin Reuptake  
Inhibitors(SSRIs)

Generic Name	Found in Brand Names
Paroxetine	Paxil, Paxil CR
Fluvoxamine	Luvox, Luvox CR
Fluoxetine	Prozac, Symbyax
Sertraline	Zoloft
Citalopram	Celexa
Escitalopram	Lexapro
Vilazodone	Viibryd

Serotonin Norepinephrine  
Reuptake Inhibitors (SSNRIs)

Generic Name	Found in Brand Names
Venlafaxine	Effexor, Effexor XR
Desvenlafaxine	Pristiq
Duloxetine	Cymbalta

Although the FDA has not received cases of serotonin syndrome to date involving vilazodone, the pharmacology of this drug places it in the SSRI category and suggests that it possesses a risk comparable to that of the SSRIs.

**II. Other psychiatric drugs with varying degrees of serotonergic activity for which the risk of serotonin syndrome with linezolid is unclear**

**Tricyclic Antidepressants (TCAs)**

Generic Name	Found in Brand Names
clomipramine	Anafranil
amitriptyline	Amitid, Amitril, Elavil, Endep, Etrafon
amitriptyline	
desipramine	
imipramine	
nortriptyline	
doxepin	Sinequan, Zonalon, Silenor
trimipramine	Surmontil

**Monoamine Oxidase Inhibitors (MAOIs)**

Generic Name	Found in Brand Names
isocarboxazid	Marplan
phenelzine	Nardil
transdermalselegiline	Emsam
tranylcypromine	Parnate

**Other Psychiatric Medications**

Generic Name	Found in Brand Names
amoxapine	Asendin
maprotiline	Ludomil
nefazodone	Serzone
trazodone	Desyrel, Oleptro, Trialodine
bupropion	Wellbutrin, Wellbutrin SR, Wellbutrin XL, Aplenzin
buspirone	Buspar

References: 1. Infectious Diseases Society of America, Arlington, VA. [http://www.idsociety.org/Stewardship\\_Policy/](http://www.idsociety.org/Stewardship_Policy/). Accessed September 2, 2015. 2. Zyvox [package insert]. Pharmacia & Upjohn Co, New York, NY; June 2015. <http://www.labeling.pfizer.com/showlabeling.aspx?id=649#section-2>. Accessed September 2, 2015. 3. US Food and Drug Administration, Silver Spring, MD. <http://www.fda.gov/Drugs/DrugSafety/ucm276251.htm>. Accessed September 2, 2015

**Take the Vaccination Pledge with your AlixaRx Clinical Pharmacist!**

Less than half of all Americans received the influenza vaccine last year. Overall, 75.2% of healthcare workers were vaccinated in the 2013-2014 season. Coverage was higher for health care workers in settings where vaccination was required (97.8%) compared to settings where vaccination was not required, but promoted (72.4%), or in settings where there was no requirement or promotion (47.9%). Over the last two years vaccination coverage has increased in all health care settings except long-term care. Additionally, health care workers in the long-term care setting had the lowest coverage at only 63%. We need to work as a team to improve vaccination participation. The vaccine is safe and recommended for everyone 6 months of age and older.

Vaccination of all employees working in long-term care is critical because our residents have a decreased response to the vaccine and are at greater risk of complications, including death from the flu. One of the best tools to protect our residents is getting vaccinated ourselves.

### Vaccines Available 2015-2016:

Standard Dose Trivalent vaccine (Fluzone™, Fluvirin™, Afluria™) is approved for ages 6 months and older. Trivalent vaccines protect against three different viruses. High Dose Trivalent Vaccine (Fluzone High Dose™) – approved for people age 65 and older. Fluzone High Dose™ was 24.2% more effective in preventing influenza than a standard dose vaccine in adult's age 65 years and older per a recent study published in the New England Journal of Medicine. Vaccine that is egg free (Flublok™ and Flucelvax™) is approved for ages 18-49 with an egg allergy. Note that Flucelvax™ should not be used in patients with a latex allergy. Quadrivalent Vaccine (Fluarix™, FluLaval™, Fluzone™, Fluzone Intradermal™) protects against two influenza A and two influenza B viruses. Different vaccines are approved for different age groups – visit the CDC website or ask your healthcare professional for details. Quadrivalent Nasal Spray (FluMist™) Vaccine is approved for use in people age 2 through 49 years old.

### Which Vaccine is best?

The CDC doesn't favor any one vaccine over another but rather recommends that everyone ages 6 months and older get vaccinated. Protect yourself and your long-term care residents by taking the CDC Vaccination Pledge at <http://www.cdc.gov/flu/nivw/pledge/index.html>.

### Storage and labeling of the Influenza Vaccines

- Storage in dormitory-style refrigerators is not recommended. The CDC strongly recommends using a compact refrigerator without a freezer compartment. Vaccines should never be stored in the door of the refrigerator. Daily temperature logs need to be within 35-46 degrees Fahrenheit.
- Label each vial with the date opened. Multi-dose vials should be discarded after 28 days unless specified otherwise by the manufacturer. The CDC notes that multi-dose influenza vials stored properly without visual changes can be used until the expiration date on the label.
- Do not use last years (2014-2015) vaccine as it is expired. Please destroy these if you have any remaining in storage.

References: 1. N Engl J Med 2014; 371:635-645 2. [www.cdc.gov](http://www.cdc.gov)

## Proposed CMS Reforms of Requirements for LTC Facilities

On July 16, 2015, CMS published proposed reforms of requirements for LTC facilities. In this article we highlight some of the proposed changes to §483.45 - Pharmacy Services and §483.80 - Infection Control.

### Pharmacy Services (§483.45)

#### Drug Regimen Review:

- In addition to the monthly drug regimen review, a pharmacist must conduct a thorough review of a resident's full medical record at least every 6 months and when the resident is new to the facility, a prior resident returns or is transferred from a hospital or other facility, and during each monthly drug regimen review when the resident has been prescribed or is taking a psychotropic drug, an antibiotic or any drug the QAA Committee has requested be included in the pharmacist's monthly drug review
- The pharmacist must document in a written report any irregularities noted during the drug regimen review that lists at a minimum, the resident's name, the relevant drug, and the irregularity identified, to be sent to the attending physician and the facility's medical director and director of nursing.

### Psychotropic Drugs:

- Define “psychotropic drug” as any drug that affects brain activities associated with mental processes and behavior. These drugs include, but are not limited to, drugs in the following categories: antipsychotics, antidepressants, anti-anxiety, hypnotic, opioid analgesics, and any other drug that results in effects similar to these drugs.
- PRN orders for psychotropic drugs be limited to 48 hours. Orders could not be continued beyond that time unless the primary care provider (for example, the resident’s physician) reviewed the need for the medications prior to renewal of the order, and documented the rationale for the order in the resident’s clinical record.

### Infection Control (\$483.80)

Develop and implement an Infection Prevention and Control Program (IPCP) that includes:

- A system for preventing, identifying, reporting, investigating, and controlling infections and communicable diseases for all residents, staff, volunteers, visitors, and other individuals providing services
- A pharmacist should be considered a potential candidate for membership in the IPCP
- Written standards, policies, and procedures must include:
  - A system of surveillance to identify possible communicable diseases/infections before they can spread
  - When and to whom possible communicable diseases /infections should be reported
  - Standard and transmission-based precautions to prevent the spread of infections
  - When isolation should be used for a resident
  - When to prohibit employees with communicable disease or infected skin lesions for direct contact with residents/food
  - Hand hygiene procedures to be followed by direct care staff

Develop and implement an Antibiotic Stewardship Program including:

- Antibiotic use protocols and a system to monitor antibiotic use
- An infection prevention and control officer (IPCO) must be a clinician who works at least part-time at the facility, has specialized training in infection prevention and control beyond their initial professional degree, and be a member of, and report regularly to, the facility’s QAPI committee
- Influenza and pneumococcal immunization program that includes
  - Education to each resident or resident’s representative regarding benefits and risks of immunization
  - Each resident is offered influenza immunization October 1 through March 31 annually and pneumococcal immunization at least once after age 65 unless medically contraindicated or already immunized
  - The resident or resident’s representative has the opportunity to refuse immunization

Source: <https://www.federalregister.gov/articles/2015/07/16/2015-17207/medicare-and-medicaid-programs-reform-of-requirements-for-long-term-care-facilities>

#### Contributing authors

**Al Barber, PharmD, CGP** – Director of Pharmacy  
**Matt Palmer, CGP, PharmD** – AlixaRx Clinical Pharmacist  
**Jenny Rowley-Funk, RPh, CGP** – AlixaRx Clinical Pharmacist  
**Tom Richards, CGP, PharmD** – AlixaRx Clinical Pharmacist  
**Blake Griese, PharmD, JD** – Editor



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6400 Pinecrest, Suite 200  
Plano, TX 75024