Family Medicine Clinical Pharmacy Forum
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Family Medicine Clinical Pharmacy Forum is a brief bi-monthly publication from the Family Medicine clinical pharmacists distributed to faculty and residents of the Department of Family Medicine. Our intent is to provide timely information on broad-based issues of pharmacotherapy, as well as regulatory and practiced-based issues affecting you as a prescriber. If you have suggestions for things you would like to see, please contact us.

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New Drugs

Telavancin (Vibativ®) and Ceftobiprole (Zeftera®)
Two new antibiotics, telavancin and ceftobiprole, have been developed to allow for more choices in infectious disease pharmacotherapy.

Ceftobiprole is under FDA review, but has already been approved in Canada. It has a spectrum similar to the third/fourth generation cephalosporins, but is extended to include MRSA which is a characteristic that makes it unique from all other cephalosporins.

Telavancin is a new glycopeptide antibiotic (the class that includes vancomycin) manufactured by Astellas, Inc. and was approved on September 11th of this year. It has an advantage over vancomycin in that it is infused once daily, but has a similar spectrum and side effect profile. Telavancin exhibits concentration-dependent bactericidal activity, whereas vancomycin efficacy is concentration-independent. The mechanism of action of telavancin is cell wall inhibition, as is that of vancomycin, but telavancin has additional activity disrupting intact bacterial membranes. There are no recommendations yet for monitoring telavancin levels.

Telavancin is renally eliminated and has dosage adjustments for patients with creatinine clearance of less than 50 ml/min (Cockroft-Gault). Patients with creatinine clearance over 50 mL/min, dosing is recommended at 10 mg/kg every 24 hours. At 30-50 mL/min dosage should be decreased to 7.5 mg/kg every 24 hours. Dosing interval is decreased to 10 mg/kg every 48 hours for patients with a creatinine clearance of 10 - 30 ml/min.
A potential for cross-resistance with VRE isolates is mentioned in the prescribing information, although actual incidence was not. Telavancin is approved for use treating skin and skin structure infections in adults.

Clinical Infectious Disease 2007;45(Suppl 3):S184-S190

**Prasugrel (Effient®)**

An oral antiplatelet drug, prasugrel is a thienopyridine prodrug that belongs to the same class as clopidogrel (Plavix®). It is currently approved for use in patients with unstable angina or MI who undergo PCI

Prasugrel possesses more efficient metabolism allowing more active metabolite action on platelet function. This translates into more inhibition of platelet activity compared to clopidogrel and ticlopidine however the risk of bleeding is also more pronounced.

TRITON-TIMI 38 was a comparison study of prasugrel to clopidogrel in patients with acute coronary syndrome undergoing elective PCI. Prasugrel significantly reduced the risks of recurrent MI and stent thrombosis. There were no significant differences in stroke incidence or cardiovascular death. An increase risk for bleeding was apparent in three subgroups: the elderly (≥75 years of age), low body weight (<60 kg), and those with previous TIA/stroke. In addition, bleeding risk is higher in those who underwent CABG. The concern for bleeding has led to a black box warning in the product labeling. It is a contraindication to use in those with prior TIA/CVA, use with caution in those ≥75 years of age unless high risk (diabetes or previous MI), and those who undergo CABG should have prasugrel discontinued for 7 days prior to surgery which will limit the use for this particular population.

Available at 5- and 10 mg doses, treatment is initiated with 60 mg loading dose followed by 10 mg per day (consider 5 mg per day in those <60 kg). Patients should also take aspirin 75-325 mg per day. The duration of use is up to 15 months at this point.

Although more effective than clopidogrel, prasugrel has some unknowns at this point and will likely be preferred for those receiving either bare metal or drug eluting stents. Routine use in the emergency department as part of the initial medical management in those presenting with acute coronary syndrome is currently under study. Until these results are known, widespread use should be avoided.

Circulation 2009;119:2758-2764
Effient® product labeling, Daiichi Sankyo, Inc, July 2009
2009 H1N1

Name changes have led to confusion this influenza season. What started out as the swine flu changed to the novel H1N1 and currently is referred to as the 2009 H1N1.

As a reminder, the seasonal influenza vaccine contains three influenza viruses: regular seasonal influenza A (an H1N1 type which is NOT the 2009 H1N1), H3N2, and type B. The 2009 H1N1 vaccine is anticipated to be available in mid-October 2009.

Treatment recommendations have been provided by the CDC for those presenting with traditional influenza as well as the 2009 H1N1. At this point, those presenting with the 2009 H1N1 are treated in a similar fashion as those presenting with the seasonal influenza as the patient populations place them at high risk for complications. The resistance patterns for the 2009-2010 seasonal influenza are not known thus changes may be forthcoming as the seasonal influenza hits.

Target groups for influenza-related complications:

- Children younger than 5 years old. However, the risk for severe complications from seasonal influenza is highest among children younger than 2 years old.
- Adults 65 years of age or older
- Pregnant women
- Persons with the following conditions:
  - Chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), neurologic, neuromuscular, or metabolic disorders (including diabetes mellitus);
  - Immunosuppression, including that caused by medications or by HIV;
- Persons younger than 19 years of age who are receiving long-term aspirin therapy, because of an increased risk for Reye syndrome.

Use of antiviral agents

1. Recommendations may change as more information becomes available and resistance patterns are updated
2. ~98% of recent circulating H1N1 virus strains were susceptible to oseltamivir or zanamivir as most of the current strains are of the novel type
3. Recommendations for treatment (use in addition to clinical judgment):
   - Treatment is recommended for all hospitalized patients with confirmed or suspected 2009 novel H1N1 or seasonal influenza
   - Treatment is generally recommended for patients who are at higher risk for influenza-related complications (as outlined above in target groups)
   - Treatment should be initiated empirically when the decision is made to treat patients who have illnesses that are clinically compatible with...
influenza. Treatment should not await laboratory confirmation because laboratory testing can sometimes delay treatment and because a negative rapid test does not rule out influenza.

4. Initiation of treatment
   - Evidence is strongest with initiated within 48 hours of onset of symptoms
   - Hospitalized patients may still receive benefit if treatment initiated beyond 48 hours

5. Duration of treatment
   - General recommendation is 5 days
   - Hospitalized patients or those with severe infection may require longer courses of therapy

6. Treatment options (will vary depending on viral surveillance data)
   - Interim recommendations based on laboratory tests and surveillance data from 2008-2009 season
   - These are subject to change as new surveillance data becomes available or local resistance patterns suggest

<table>
<thead>
<tr>
<th>Rapid antigen or other laboratory test</th>
<th>Predominant virus(es) in community</th>
<th>Preferred medication(s)</th>
<th>Alternative (combination antiviral treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not done of negative, but clinical suspicion for influenza</td>
<td>H1N1 or unknown</td>
<td>Zanamivir</td>
<td>Oseltamivir + Rimantadine*</td>
</tr>
<tr>
<td>Not done of negative, but clinical suspicion for influenza</td>
<td>H3N2 or B</td>
<td>Oseltamivir or Zanamivir</td>
<td>None</td>
</tr>
<tr>
<td>Positive A</td>
<td>H1N1 or unknown</td>
<td>Zanamivir</td>
<td>Oseltamivir + Rimantadine*</td>
</tr>
<tr>
<td>Positive A</td>
<td>H3N2 or B</td>
<td>Oseltamivir or Zanamivir</td>
<td>None</td>
</tr>
<tr>
<td>Positive B</td>
<td>Any</td>
<td>Oseltamivir or Zanamivir</td>
<td>None</td>
</tr>
<tr>
<td>Positive A+B</td>
<td>H1N1 or unknown</td>
<td>Zanamivir</td>
<td>Oseltamivir + Rimantadine</td>
</tr>
<tr>
<td>Positive A+B</td>
<td>H3N2 or B</td>
<td>Oseltamivir or Zanamivir</td>
<td>None</td>
</tr>
</tbody>
</table>

*Amantadine can be substituted for rimantadine but has increased risk of adverse events. Human data are lacking to support the benefits of combination antiviral treatment of influenza;

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Special thanks to Claire Sauter, PharmD Candidate, for help with this issue
however, these interim recommendations are intended to assist clinicians treating patients who might be infected with oseltamivir-resistant influenza A (H1N1) virus.

**Positive A+B indicates a rapid antigen test that cannot distinguish between influenza and influenza B viruses

Please see [www.cdc.org](http://www.cdc.org) for updated information

**Inhaler expiration dates**
The expiration dates on stock bottles of medications apply with the assumption that medications are stored correctly and the package is unopened. As with insulins, it is important to understand the differences in expiration dates once inhalers are dispensed. Many of the newer inhalers will come in foil wrapping in which case the expiration is on the packaging. Once the inhaler is removed from the foil wrapping, the expiration date will vary depending on the product. Here is a table listing the expiration dates once the inhaler is removed from the foil wrapping:

<table>
<thead>
<tr>
<th>Inhaler</th>
<th>Expiration Date Once Removed from Wrapping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventolin HFA (200 actuations)</td>
<td>6 months</td>
</tr>
<tr>
<td>Ventolin HFA (60 actuations)</td>
<td>12 months</td>
</tr>
<tr>
<td>Symbicort</td>
<td>90 days</td>
</tr>
<tr>
<td>Advair Diskus</td>
<td>1 month</td>
</tr>
<tr>
<td>Ásmanex Twisthaler</td>
<td>45 days</td>
</tr>
<tr>
<td>Foradil</td>
<td>4 months</td>
</tr>
<tr>
<td>Flovent Diskus 50 mcg</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Flovent Diskus 100 mcg</td>
<td>2 months</td>
</tr>
<tr>
<td>Flovent Diskus 250 mcg</td>
<td>2 months</td>
</tr>
<tr>
<td>Proair HFA</td>
<td>These do not come in foil wrappers thus expiration date is good for 2 years from manufacturing date</td>
</tr>
<tr>
<td>Proventil HFA</td>
<td></td>
</tr>
</tbody>
</table>

Pharmacist’s Letter 2009;25:50

**Colchicine dosing**

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Special thanks to Claire Sauter, PharmD Candidate, for help with this issue
Although not considered first line, the dosing of colchicine for treatment of acute gout has changed in part due to a new FDA-approved version called Colcrys®. The old method for dosing was 2 of the 0.6 mg tablets initially followed by 1 tablet every hour until pain subsided or GI toxicity occurred. This would routinely lead to toxicity and patient intolerance. The new dosing is 2 tablets initially followed by 1 tablet an hour later for a gout flare. Efficacy is the same as the old method and GI toxicity has been reduced by this new dosing scheme.