Indiana Drug Utilization Review Board

January 1999 Vol. 2 / Issue 1

Treatment of Otitis Media

With the prevalence of drug resistant Streptococcus pneumoniae appearing in community-acquired infections, a report is expected to be published from a Center for Disease Control (CDC) working group. The group will recommend the dose of amoxicillin for the treatment of otitis media in children to increase from 40mg/kg/day to higher doses of 60-90mg/kg/day. This decision by the CDC is based on the emerging resistance problem in S. pneumoniae, a common bacterial pathogen in acute otitis media in young children. The higher dose will increase the amoxicillin concentrations in the middle ear fluid to levels that exceed the MIC for intermediate and resistant strains of S. pneumoniae[1]. The CDC group, consisting of "opinion leaders" associated with otitis media, discussed the treatment of acute otitis media caused by resistant strains of S. pneumoniae and developed guidelines based on this rising concern. Recommendations include continuation of amoxicillin as the first-line agent in the empiric treatment of acute otitis media, but dosed at 60-90 mg/kg/day. Amoxicillin/clavulanate, cefuroxime axetil are recommended for second-line therapy. Cefpodoxime proxetil is another possible second-line agent, although its effectiveness against pneumococci is less than amoxicillin/clavulanate and cefuroxime. Cefpodoxime proxetil demonstrates greater effectiveness against H. influenza than do the other two agents. When treatment failures to first and second-line agents occur, the use of IV/IM ceftriaxone for 2-3 days, oral clindamycin, or oral amoxicillin/clavulanate with additional amoxicillin to achieve a total daily dose of 80-90mg/kg amoxicillin, would be warranted[2].

Prescribers should be aware of the susceptibility of isolates presented in their geographic region, as well as their patient's history, lifestyle, and recent antimicrobial use, when determining drug treatment in a child diagnosed with acute otitis media. In situations where the likelihood of penicillin-intermediate to penicillin-resistant S. pneumonia is the cause, higher doses of amoxicillin are recommended. Parents of these children should be counseled to increase their child's fluid intake in order to prevent crystalluria and to watch for signs of diarrhea; although the likelihood of diarrhea is no more prevalent in higher doses than in normal doses of amoxicillin[1].

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[1] Levien TL, Baker DE. Amoxicillin Dose in Otitis Media. Pharmacist's Letter, 1998; Document #131202:1-3.

[2] Poole MD. Declining Antibiotic Effectiveness in Otitis Media – A Convergence of Data. Ear, Nose and Throat Journal, 1998; 77:444, 446-7. (http://id.medscape.com/Medquest/ENT/1998/v77.n06/ent7706.08.html)

The Indiana Drug Utilization Review Newsletter is prepared by the Indiana DUR Board, Office of Medicaid Policy and Planning and EDS. Any comments or suggestions should be forwarded to:

Indiana DUR Board
402 West Washington St.
Room W382
Indianapolis, Indiana 46204

Mark Your Calendar: The next Indiana DUR Board meeting will be held on March 12, 1999, at 9:30AM in room W-451 of the Indiana State Government Center South

Drug-Food Interaction with Grapefruit Juice

Recent attention by the Joint Commission on Accreditation of Healthcare Organizations, the Food and Drug Administration, the National Institute of Health, and other organizations on the potential interactions caused by food on medication therapy has prompted several studies and journal articles on the subject. The Indiana Medicaid DUR Board would like to alert prescribers and pharmacy providers on the potential drug-food interactions related to grapefruit juice.

Cytochrome P-450 enzymes represent one of the most important mechanisms responsible for the metabolism of many drugs. Products that induce or inhibit the quantities of these enzymes can alter the effectiveness of the cytochrome P-450 system. Medications such as phenytoin, phenobarbital, and isoniazid are cytochrome P-450 enzyme inducers. Inducers enhance the metabolism of other drug products that share the same enzymatic pathways, thereby decreasing the bioavailability of those drugs and decreasing their effectiveness. Erythromycin, fluconazole, and ritonavir inhibit cytochrome P-450 enzymes that decrease the metabolic rate of other medications and increase the bioavailability of those drugs, resulting in enhanced pharmacologic effects[1].

Researchers have identified compounds in grapefruit juice that have been found to inhibit Cytochrome P-450 enzymes; specifically, CYP1A2, CYP3A3, and CYP3A4. As a result, a single glass of grapefruit juice, taken with certain medications, has been observed to increase the absorption and bioavailability of those medications. The pharmacologic effects of these drugs are then enhanced in the body, increasing the likelihood of side effects associated with drug toxicity. Researchers from the University of Michigan Medical Center in Ann Arbor determined the main effect from grapefruit juice originates from its ability to decrease the amount of the enzyme, CYP3A4 that is present in the small intestine[2]. Inhibition of the CYP3A4 enzyme results in an increase in absorption rate, maximal plasma concentration (Cmax), time to maximal plasma concentration (tmax), and area under the plasma concentration time curve (AUC) of those drugs affected by the enzyme. Since no changes have been observed in the pharmacokinetic parameters of these drugs' total body clearance, elimination half-life (T1/2), or volume of distribution, experts agree that inhibition of the CYP3A4 enzyme in the intestine is the predominant cause of interactions between grapefruit juice and medications[3].

The medications affected by coadministration with grapefruit juice include:

- Calcium channel blockers – felodipine, nifedipine, nimodipine, and verapamil.
- Cyclosporine
- Benzodiazepines – Oral products only.
- Terfenadine
- Protease Inhibitors
- Estrogen products

Counseling patients about the potential risks of taking grapefruit juice with their medication may avoid the occurrence of harmful adverse drug reactions.

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[1] Buck, ML. The Cytochrome P450 Enzyme System and Its Effect on Drug Metabolism. Pediatric Pharmacotherapy, 1997; 3. (http://id.medscape.com/UVA/PedPharm/1997/v03.n05/pp0305.html)

[2] National Institutes of Health. Drug Benefit Trends. 1997; 9:35-8.

[3] Rodvold, KA, Meyer, J. Drug-Food Interactions with Grapefruit Juice. Infections in Medicine, 1996; 13: 868, 871-873, 912. (http://www.medscape.com/SCP/IIM/1996/v13.n10/m1741.rodvold/m1741.rodvold.html)

Prescribers to Include License Number on Prescriptions

The Indiana Medicaid DUR Board wishes to remind prescribers that they must include their Indiana state medical license numbers on prescriptions written to Medicaid recipients for legend and non-legend drug products. This requirement is in addition to State regulations that already request prescribers' license numbers on prescriptions written to the public for controlled substances (Ref. 856 IAC 1-34). Indiana Medicaid policy requires pharmacy providers to include the state license number of the prescribing physician on each claim submitted to the program for payment. Including prescribers' state license numbers on written prescriptions helps pharmacy providers submit and maintain accurate records and claims by enhancing the identification of those prescribing physicians, especially for those in multi-physician practices. Accurate claim data also assists the DUR Board in communicating with the correct prescriber for information related to Retrospective Drug Utilization and Review (RetroDUR) activities.

Indiana Medicaid DUR Board Report
Top 25 Legend Drugs by **Total Paid Claims**
1st Quarter - Calendar Year 1998

RANKING	NDC	DRUG NAME	STRENGTH	DOSAGE FORM	**TOTAL PAID CLAIMS**	NUMBER OF CLAIMS	AVERAGE QUANTITY	AVERAGE CLAIM AMOUNT
1	**61113-0742**	**Prilosec**	**20 MG**	**Capsule**	**$1,852,661**	**15,725**	**35**	**$117.82**
2	**00002-4117**	**Zyprexa**	**10 MG**	**Tablet**	**1,531,585**	**5,134**	**42**	**298.32**
3	**00777-3105**	**Prozac**	**20 MG**	**Pulvule**	**1,134,151**	**11,859**	**44**	**95.64**
4	**00944-2938**	**Recombinate**	**1020 AHFU**	**Vial**	**985,779**	**145**	**6,518**	**6,798.47**
5	**00300-3046**	**Prevacid**	**30 MG**	**Capsule**	**627,377**	**5,882**	**34**	**106.66**
6	**00002-3144**	**Axid**	**150 MG**	**Pulvule**	**592,040**	**8,045**	**52**	**73.59**
7	**00074-6215**	**Depakote**	**500 MG**	**Tablet**	**524,739**	**5,201**	**88**	**100.89**
8	**00078-0127**	**Clozaril**	**100 MG**	**Tablet**	**498,007**	**5,233**	**30**	**95.17**
9	**00049-4900**	**Zoloft**	**50 MG**	**Tablet**	**472,105**	**7,015**	**34**	**67.30**
10	**00002-4115**	**Zyprexa**	**5 MG**	**Tablet**	**471,069**	**2,689**	**37**	**175.18**
11	**50458-0330**	**Risperdal**	**3 MG**	**Tablet**	**461,998**	**2,135**	**56**	**216.39**
12	**00053-7668**	**Mononine**	**1 MU**	**Vial**	**460,745**	**58**	**8,033**	**7,943.87**
13	**50458-0300**	**Risperdal**	**1 MG**	**Tablet**	**452,180**	**5,230**	**44**	**86.46**
14	**00029-3211**	**Paxil**	**20 MG**	**Tablet**	**424,146**	**6,217**	**35**	**68.22**
15	**58394-0001**	**Benefix**	**1 MU**	**Vial**	**405,310**	**54**	**7,218**	**7,505.75**
16	**00049-4910**	**Zoloft**	**100 MG**	**Tablet**	**402,215**	**5,298**	**38**	**75.92**
17	**00006-0963**	**Pepcid**	**20 MG**	**Tablet**	**385,906**	**5,405**	**49**	**71.40**
18	**00045-0659**	**Ultram**	**50 MG**	**Tablet**	**365,122**	**9,072**	**62**	**40.25**
19	**50458-0430**	**Propulsid**	**10 MG**	**Tablet**	**336,686**	**5,204**	**100**	**64.70**
20	**50458-0320**	**Risperdal**	**2 MG**	**Tablet**	**302,328**	**1,844**	**50**	**163.95**
21	**55953-0544**	**Ranitidine**	**150 MG**	**Tablet**	**297,727**	**4,792**	**56**	**62.13**
22	**00074-2586**	**Biaxin**	**500 MG**	**Tablet**	**290,864**	**4,858**	**20**	**59.87**
23	**00085-0458**	**Claritin**	**10 MG**	**Tablet**	**279,739**	**5,092**	**28**	**54.94**
24	**00074-6214**	**Depakote**	**250 MG**	**Tablet**	**276,801**	**4,738**	**91**	**58.42**
25	**00071-0805**	**Neurontin**	**300 MG**	**Tablet**	**271,473**	**2,636**	**110**	**102.99**

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RANKING	NDC	DRUG NAME	STRENGTH	DOSAGE FORM	TOTAL PAID CLAIMS	**NUMBER OF CLAIMS**	AVERAGE QUANTITY	AVERAGE CLAIM AMOUNT
1	**61113-0742**	**Prilosec**	**20 MG**	**Capsule**	**$1,852,661**	**15,725**	**35**	**$117.82**
2	**00378-0155**	**Propoxy-N/ APAP**	**100/650 MG**	**Tablet**	**85,966**	**12,861**	**52**	**6.68**
3	**59930-1560**	**Albuterol**	**90 MCG**	**Inhaler**	**150,350**	**12,246**	**20**	**12.28**
4	**00777-3105**	**Prozac**	**20 MG**	**Pulvule**	**1,134,151**	**11,859**	**44**	**95.64**
5	**00045-0659**	**Ultram**	**50 MG**	**Tablet**	**365,122**	**9,072**	**62**	**40.25**
6	**52544-0349**	**Hydrocod/ APAP**	**5/500 MG**	**Tablet**	**49,128**	**8,925**	**40**	**5.50**
7	**00085-0787**	**K-Dur**	**20 MEQ**	**Tablet**	**217,657**	**8,756**	**56**	**24.86**
8	**00071-0362**	**Dilantin**	**100 MG**	**Kapseal**	**210,908**	**8,300**	**106**	**25.41**
9	**00002-3144**	**Axid**	**150 MG**	**Pulvule**	**590,040**	**8,045**	**52**	**73.59**
10	**00378-0216**	**Furosemide**	**40 MG**	**Tablet**	**37,401**	**7,999**	**50**	**4.68**
11	**00046-0867**	**Premarin**	**0.625 MG**	**Tablet**	**121,482**	**7,303**	**36**	**16.63**
12	**00049-4900**	**Zoloft**	**50 MG**	**Tablet**	**472,105**	**7,015**	**34**	**67.30**
13	**00069-3060**	**Zithromax**	**250 MG**	**Tablet**	**251,817**	**6,902**	**6**	**36.48**
14	**00003-1738**	**Trimox**	**250 MG**	**Suspension**	**47,731**	**6,897**	**149**	**6.92**
15	**00173-0242**	**Lanoxin**	**0.125 MG**	**Tablet**	**45,427**	**6,569**	**32**	**6.92**
16	**00029-3211**	**Paxil**	**20 MG**	**Tablet**	**424,146**	**6,217**	**35**	**66.22**
17	**59930-1515**	**Albuterol**	**5 MG**	**Solution**	**123,992**	**6,014**	**28**	**20.62**
18	**00300-3046**	**Prevacid**	**30 MG**	**Capsule**	**627,377**	**5,882**	**34**	**106.66**
19	**00597-0082**	**Atrovent**	**18 MCG**	**Inhaler**	**196,360**	**5,520**	**17**	**35.57**
20	**00006-0963**	**Pepcid**	**20 MG**	**Tablet**	**385,906**	**5,405**	**49**	**71.40**
21	**00049-4910**	**Zoloft**	**100 MG**	**Tablet**	**402,215**	**5,298**	**38**	**75.92**
22	**00083-0027**	**Tegretol**	**200 MG**	**Tablet**	**253,476**	**5,288**	**140**	**47.93**
23	**00078-0127**	**Clozaril**	**100 MG**	**Tablet**	**498,007**	**5,233**	**30**	**95.17**
24	**50458-0300**	**Risperdal**	**1 MG**	**Tablet**	**452,180**	**5,230**	**44**	**86.46**
25	**50458-0430**	**Propulsid**	**10 MG**	**Tablet**	**336,686**	**5,204**	**100**	**64.70**

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