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DUR DIGEST

The Bulletin of Medicaid Drug Utilization Review in Iowa

Inappropriate Pediatric Antibiotic Prescribing in Ambulatory Setting

Antibiotics are among the most commonly prescribed medications in pediatric patients, with more than 30 million prescriptions written annually. Rates of antibiotic prescribing in ambulatory settings have been declining, yet antibiotic overuse continues, contributing to the development of antibiotic-resistant pathogens, unnecessary costs, and avoidable adverse events. In December 2011, *Pediatrics* published an article examining antibiotic prescribing patterns in ambulatory pediatric patients in the United States. Two nationwide databases were analyzed, looking at visits to offices, outpatient departments, and emergency departments by children younger than 18 years from 2006 to 2008.

Antibiotics were prescribed in an estimated 49 million pediatric ambulatory visits. Broad-spectrum antibiotics were prescribed in 50% of these visits, with macrolides prescribed most often, followed by broad-spectrum cephalosporins. The most common visit was for respiratory conditions (72%) in which antibiotics were prescribed. Prescriptions for broad-spectrum antibiotics were highest (63%) for acute respiratory tract infections for which antibiotics were not indicated (such as for nasopharyngitis, bronchitis, viral pneumonia, and influenza). It is estimated that 2.1 million prescriptions are written for bronchitis annually.

References:

Hersh AL et al. Antibiotic prescribing in ambulatory pediatrics in the United States. Pediatrics 2011 Dec; 128:1053.

Vitamin E Supplements Linked to Increase in Prostate Cancer Risk

There is an increased risk of prostate cancer in healthy middle-aged and older men who take vitamin E supplements according an update to the SELECT (Selenium and Vitamin E Cancer Prevention Trial) trial. The study included over 35 thousand North American men aged 50 years or older if black or 55 years or older if of other races/ethnicities. Those that had an average risk of prostate cancer were randomized into four groups: Vitamin E (400 IU per day, all rac-alpha-tocopherol acetate), selenium (200 mcg per day), the combination of vitamin E and selenium, or a placebo. When the trial was halted 5.5 years after starting due to treatment futility, men in the vitamin E group had a slightly increased risk of prostate cancer compared to men in the placebo group. But, 1.5 years after the trial had been stopped (follow-up 7 years after trial was initiated), those that took vitamin E (400 IU daily) had a 17% greater risk of prostate cancer than those that took placebo, indicating the effect of vitamin E continues even after discontinuation. It is not know how vitamin E increases prostate cancer and more studies are needed to determine the cause. Interestingly, men who took vitamin E with selenium did not have any significant increase in the risk of prostate cancer. It is unknown why adding selenium to vitamin E eliminates the risk of prostate cancer.

JAMA 2011;306:1549-56

Antipsychotics in Iowa Medicaid Children

The use of antipsychotic agents has increased greatly over the past decade, specifically in children and adolescents.[1] In the United States, from 1993 to 2002, outpatient antipsychotic use for patients age 20 years and younger increased approximately 6-fold.[2] Recently there has been increased public scrutiny, controversy, and debate regarding the escalating use of antipsychotic agents in children and the absence of data on long-term effects.[3] The majority of outpatient pediatric prescriptions, including psychotropics, are used off label.[4] The long-term efficacy and safety of second generation antipsychotics, as well as other psychotropics, has not been well established for a clinical indication.

The DUR reviewed a letter from the Department of Health and Human Services (HHS) dated November 23, 2011 at the December 2011 DUR meeting regarding the effective use of psychotropic medications among children in foster care. The DUR came to the consensus that this issue should be addressed within the entire Iowa Medicaid population. The letter addressed specific issues; polypharmacy and limited studies for the safety and efficacy for use of these medications in children. The letter went on to further recommend states use their Drug Utilization Review (DUR) programs to monitor dispensing at the point of service and influence prescriber behavior. Suggestions include system edits to limit inappropriate dosage and polypharmacy. The DUR is currently working on strategies to address this issue and will be obtaining input from the Mental Health Advisory Group during this process.

Recently, the DUR Commission reviewed pharmacy claims data for members 0 through 17 years of age with claims for two or more antipsychotics concurrently for 45 or more days from September 1, 2011 through November 30, 2011. There were a total of 142 members identified.

Number of Members Aged 0 Through 17 Years with Multiple Antipsychotics for ≥ 45 days

Age (Years)	N of Members	N of Prescribers
0-5	5	6
6-11	30	37
12-17	107	61

The DUR Commission determined letters should be sent to the prescribers of the 142 members asking if the patient had experienced multiple failures with several monotherapy trials with an antipsychotic prior to using multiple antipsychotics. Results of this educational initiative will be brought to a future DUR meeting.

References:

1. Vitiello B, Correll C, Van Zwieten-Boot, Zuddas A, Parellada M, Arango C. Antipsychotics in children and adolescents: Increasing use, evidence for efficacy and safety concerns. Eur Neuropsychopharmacol. 2009 May 23, Epub.
2. Olfson M, Blanco C, Liu L, Moreno C, Laje G. National trends in the outpatient treatment of children and adolescents with antipsychotic drugs. Arch Gen Psychiatry. 2006; 63:679-685. Abstract
3. Parens E, Johnston J. Understanding the agreements and controversies surrounding childhood psychopharmacology. Child Adolesc Psychiatry Ment Health. 2008; 2:5.
4. Bazzano AT, Mangione-Smith R, Schonlau M, Suttorp MJ, Brook RH. Off-label prescribing to children in the United States outpatient setting. Acad Pediatr. 2009;9:81-88. Abstract

FDA Updates and New/Updated Drug PA Criteria

FDA Update

The U.S. Food and Drug Administration (FDA) has announced that proton pump inhibitors (PPIs) may be associated with an increased risk of Clostridium difficile-associated diarrhea (CDAD). The FDA reviewed reports of PPI-associated CDAD from the FDA Adverse Event Reporting System and from the medical literature. The association of PPI use and CDAD varied among studies, ranging from a risk of 1.4 to 2.75 higher in those exposed to a PPI compared to those without PPI exposure. Many of the cases reported involved patients who were elderly, had chronic and/or underlying conditions, or were taking broad-spectrum antibiotics, all of which could have increased the risk of CDAD. In spite of potential predisposition to CDAD, or other limitations to study design, association with PPI use could not be ruled out and patients with these risk factors may have more serious outcomes from CDAD associated with PPI use. The FDA is working with manufacturers to include information regarding the increased risk of CDAD with use of PPIs in their prescribing information and is also evaluating the risk of CDAD in users of histamine H2 receptor blockers.

The FDA is evaluating postmarketing reports of serious bleeding events in patients taking *Pradaxa* (dabigatran etexilate mesylate), indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. The FDA is working to determine whether reports of bleeding in patients taking *Pradaxa* are occurring more commonly than would be expected. The FDA continues to believe that *Pradaxa* provides an important health benefit when used as directed and recommends that health care providers follow the recommendations in the approved drug label. Patients should not stop taking *Pradaxa* without talking to their health care provider.

The FDA has added new safety alerts to the prescribing information for statins, citing rare risks of memory loss, diabetes, and muscle pain. Among the drugs affected are *Lipitor* (atorvastatin), *Zocor* (simvastatin), *Crestor* (rosuvastatin), and *Vytorin* (ezetimibe/simvastatin). The FDA said the new alerts should not discourage patients from taking statins and that patients with diabetes, or who develop diabetes while taking statins, should continue taking the medicine.

New Drug Prior Authorization Criteria

Roflumilast (Daliresp™)

Prior authorization is required for roflumilast (Daliresp™). Payment will be considered for patients 18 years of age or older when the following is met:

1. A diagnosis of severe COPD with chronic bronchitis as documented by spirometry results, and
2. A smoking history of ≥ 20 pack-years, and
3. Currently on a long-acting bronchodilator in combination with an inhaled corticosteroid with documentation of inadequate control of symptoms, and
4. A history of at least one exacerbation in the past year requiring treatment with oral glucocorticosteroids.

The required trials may be overridden when documented evidence is provided that the use of these agents would be medically contraindicated.

Dextromethorphan and Quinidine (Nuedexta™)

Prior authorization is required for Nuedexta™. Payment will be considered under the following conditions:

1. Patients must have a diagnosis of pseudobulbar affect (PBA) secondary to amyotrophic lateral sclerosis (ALS) or multiple sclerosis (MS).
2. A trial and therapy failure at a therapeutic dose with amitriptyline or an SSRI.
3. Initial authorizations will be approved for 12 weeks with a baseline Center for Neurologic Studies Lability Scale (CNS-LS) questionnaire.
4. Subsequent prior authorizations will be considered at 6 month intervals with documented efficacy as seen in an improvement in the CNS-LS questionnaire.

DUR Activities

Medicaid Statistics for Prescription Claims

from October 1, 2011 to December 31, 2011*

Number of claims paid: 1,142,899

Total dollars paid: $69,078,933.52

Percent controlled substances: 18.43%

Average amount paid per claim: $60.44

Average amount paid per claim, brand: $221.19

Average Amount paid per claim, generic: $12.15

Top Drugs by Number of Prescriptions	Top Drugs by Dollars Spent	Top Therapeutic Class by Dollars Spent
ProAir HFA $48.16/RX	*Concerta* 36mg $1,306,550 $235.00/RX	Antipsychotics – Atypicals $12.2 million
Hydrocodone/APAP 5-500 $4.78/RX	*Abilify* 5mg $1,216,907 $432.60/RX	Stimulants – Amphetamines – Long Acting $4.6 million
Lexapro 20mg $106.75/RX	*Synagis 100mg/ml* $853,782 $2571.63/RX	Stimulants – Methylphenidate-Long Acting $3.6 million
APAP 325mg $5.18/RX	*Concerta 54mg* $918,150 $270.63/RX	Antidepressants – Selected SSRIs $3.2 million
Concerta 36mg $235.00/RX	*Abilify 10mg* $927,438 $450.65/RX	Anticonvulsants $3.1 million

*All dollars reported are Pre-Rebate