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Indiana Medicaid DUR Board
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Indiana Medicaid Drug Utilization Review Board Newsletter

Metered-Dose Inhaler Study

A recent study in *Clinical Therapeutics* suggests that treatment costs of asthma may be reduced by approximately 16% for patients using metered-dose inhalers, by switching from traditional metered-dose inhalers to breath-actuated inhalers. Researchers analyzed records of 13,000 asthma patients. They concluded that the average annual cost for asthma treatment was \$108 less, per patient, among users of breath-actuated inhalers. The study reports that costs for emergency room visits and hospitalizations were approximately 35% lower for these patients. The study also compared costs for patients using albuterol in press and breath inhalers with patients receiving pirbuterol in breath-actuated inhalers (Maxair Autohaler). The study was funded by 3M, manufacturer of Maxair.¹



¹ Clin Thera 1999; 21:236-253.

Serotonin Syndrome: Cause, Symptoms, and Prevention

Recent reports in literature have drawn attention back to the increase in the incidences of serotonin syndrome. Although the syndrome was first identified several decades ago in animal studies using monoamine oxidase inhibitors and tryptophan in rodents², it is occurring in patient populations at a greater frequency with the increased use of other pharmacological agents that affect the serotonergic pathways. Within the last decade, the United States has seen a dramatic influx of new products on the market that specifically affect the serotonin concentrations in the body. The increased utilization of these products coincide with the evolving belief that the pathophysiology of almost every major psychiatric disease likely involves serotonin. While the majority of serotonin syndrome cases are mild and reversible, the occurrence can lead to significant complications and even death.

Serotonin syndrome can be caused by various combinations of drugs, but typically results

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² Sporer, Karl A. The Serotonin Syndrome; Implicated Drugs, Drug Safety 1995; 13 (2): 94-104.

This newsletter has been prepared by the Indiana Medicaid DUR Board, the OMPP and EDS. Please forward any comments or suggestions to the Indiana Medicaid DUR Board.

from a combination of serotonergic agents that have different mechanisms of action.³ Serotonergic drugs exert their effects on serotonin concentrations in the body by the following mechanisms:^{2,4}

- They increase the synthesis of serotonin in the body. L-tryptophan is a drug product when ingested is metabolized to serotonin in the body.
- They decrease serotonin metabolism. Monoamine oxidase inhibitors prevent the intracellular destruction of serotonin and allow increased levels to accumulate.
- They increase the release of serotonin. Drug products such as amphetamines, cocaine, and reserpine increase the release of serotonin in the synapse.
- They inhibit serotonin uptake. Once serotonin is released in the synapse, its function is rapidly terminated by its presynaptic re-uptake back into the neuron. Drugs such as tricyclic antidepressants and selective serotonin reuptake inhibitors prolong the exposure of serotonin in the synapse to the post-synaptic receptors. Other drug products that may function in the same manner include amphetamines, cocaine, dextromethorphan, meperidine and venlafaxine.

- They are direct serotonin receptor agonists. Drug products exist that stimulate the post-synaptic serotonin receptors to elicit their therapeutic effects. Buspirone stimulates a specific serotonin receptor subtype (5-HT_{1A}) that is believed to have anxiolytic and antidepressant effects. Sumatriptan stimulates a different serotonin receptor subtype (5-HT_{1D}) that has been found outside the central nervous system on cephalic blood vessels, which elicits an antimigraine effect. Ondansetron stimulates a different serotonin receptor subtype (5-HT₃) that is found near the emesis centre, which elicits an antiemetic effect.

Other mechanisms have also been proposed as being involved in the etiology of this syndrome.

Defects in monoamine metabolism, as well as acquired diseases such as liver or pulmonary insufficiency, may contribute to the development of this process.³

The serotonin syndrome has been characterized by a collection of at least three of the following symptoms and usually takes place around a recent addition or dosage increase of a serotonergic drug product:²

1. Mental status change
2. Agitation
3. Myoclonus
4. Hyperreflexia

5. Fever
6. Shivering
7. Diaphoresis
8. Ataxia
9. Diarrhea

The onset of the serotonin syndrome ranges from minutes after receiving another serotonergic agent, to weeks after a stable dosage. The majority of serotonin syndrome cases are mild and will readily respond to withdrawal of the serotonergic drugs and supportive treatment. Mild cases require hospitalization, controlling the hyperreflexia and myoclonus with benzodiazepines and possibly propranolol. Acetaminophen may be used if fever is present. Symptoms usually resolve in six to twelve hours and most will completely resolve within 24 hours. The appearance of a fever > 105° F usually indicates a severe disease process, with significant

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mortality and complication rates. These patients require aggressive treatment to control the hyperthermia. In order to prevent the

occurrence of serotonin syndrome, several steps may be taken which decrease the probability that it will affect a patient:⁵

- Discontinue all serotonergic agents when possible, before

³ Micromedex. Drug Consults: Serotonin Syndrome. Micromedex, Inc. Volume 94.

⁴ Kehoe, William A. Update on Adverse Reactions to SSRI Antidepressants. Pharmacist's Letter Document #140615.

⁵ Gravlin, Michelle A. Serotonin Syndrome: What Causes It, How To Recognize It, And Ways to Avoid It. Hospital Pharmacy, 1997; 42 (4): 570-575.

beginning other agents that can increase serotonin concentrations. Paroxetine, sertraline, venlafaxine, and nefazodone need 5 to 7 days to wash out of the system prior to beginning other serotonergic agents.

Fluoxetine should be discontinued 5 weeks in advance due to its norfluoxetine active metabolite, and monoamine oxidase inhibitors need 4 weeks to wash out of the system before administering other serotonergic agents.

- Educate patients receiving serotonergic agents about the symptoms of serotonin syndrome, the need to notify other prescribers about their existing drug regimen before any new medication is started, and to avoid cough medicines containing dextromethorphan (i.e. Robitussin DM) because they inhibit the presynaptic reuptake of serotonin.
- Avoid serotonergic combinations. For example: when presented with a patient complaining of insomnia and already on a serotonergic antidepressant, consideration should be directed at changing to a sedating antidepressant or using a nonserotonergic sedative such as diphenhydramine or lorazepam rather than adding trazodone.
- Be aware of the pharmacology of new agents prescribed. New antidepressants on the market exert their effects by

increasing the serotonin concentrations in the body. Serotonergic agents are very effective drug products. They do, however, have potential side effects related to their mechanisms of action that require close monitoring and assessment.

DUR Board Elects New Chairman and Vice-Chairman

A new DUR Board Chairman and Vice-Chairman were elected during the March 12, 1999 Indiana Medicaid DUR Board Meeting.

G. Thomas Wilson, R.Ph. J.D. was elected as the chairman and Patricia A Treadwell, M.D. was elected as the vice-chairman for the Indiana Medicaid DUR Board. Thomas Bright, M.D. and Sharon Hammerich, Pharm.D. had previously served as the DUR Board Chairman and vice-chairman, respectively.

Mr. Wilson received his Pharmacy Degree at Purdue University in West Lafayette, Indiana and his Law Degree from the Indiana University School of Law in Indianapolis, Indiana. He is currently a member of the Department of Pharmacy Practice, School Liaison to the Indiana Board of Pharmacy, and a lecturer in pharmacy law at Purdue University's School of Pharmacy and Pharmacal Sciences. Mr. Wilson has presented more than 140 continuing education program. He is a member of numerous associations including the American and Indiana Bar Associations; Indiana Pharmacy Alliance; American Association

DUR Board Calendar

June 11, 1999

9:30 am, Indiana Government Center, South Conference Center Room A
DUR Board Meeting

September 10, 1999

9:30 am, Indiana Government Center, South Conference Center Room 6
DUR Board Meeting

December 10, 1999

9:30 am, Indiana Government Center, South Training Center Room 1
DUR Board Meeting

For more information call Ms. Karen Baer at (317) 232-4391

of Colleges of Pharmacy; and the American Society for Pharmacy Law. He has been a member of the Indiana Medicaid DUR Board since the summer of 1997.

Dr. Treadwell received her Medical Degree from Cornell University Medical College in New York, New York. She is currently on the medical staff at Indiana University Hospitals and Wishard Memorial Hospital, and is also an Associate Professor for the Departments of Dermatology and Pediatrics. She has served as President for the Dermatology Section of the National Medical Association. Dr. Treadwell is a member of numerous associations including the Alpha Omega Alpha Medical Honor Society; American Academy of Dermatology; American Academy of Pediatrics; Indiana Dermatology Society; and the Women's Dermatologic Society. She has been a member of the Indiana Medicaid DUR Board since 1993.



Top 25 Drug Products

Based on Total Dollars Spent for 4th Quarter 1998

Rank	Drug Name/Dose/Form	Total \$ Paid	# Claims	Average Quantity	Average \$ Claim
1	Prilosec 20mg Capsule	\$2,176,123	17,633	36	\$123
2	Zyprexa 10mg Tablet	\$1,863,667	5,852	44	\$318
3	Recombinant Vials	\$1,232,796	178	6,537	\$6,926
4	Prozac 20mg Pulvule	\$1,194,034	12,240	44	\$98
5	Prevacid 30mg Capsule	\$ 946,227	8,536	34	\$111
6	Benefix 1000IU Vial	\$ 810,363	113	6,975	\$7,171
7	Depakote 500mg Tablet	\$ 672,585	6,291	86	\$107
8	Risperdal 1mg Tablet	\$ 636,305	6,956	43	\$91
9	Axid 150mg Pulvule	\$ 557,493	7,458	51	\$75
10	Zyprexa 5mg Tablet	\$ 543,518	3,053	37	\$178
11	Zoloft 50mg Tablet	\$ 519,306	7,431	35	\$70
12	Risperdal 3mg Tablet	\$ 495,640	2,322	53	\$213
13	Clozaril 100mg Tablet	\$ 484,948	3,349	47	\$145
14	Paxil 20mg Tablet	\$ 481,402	6,744	36	\$71
15	Zoloft 100mg Tablet	\$ 472,976	6,211	37	\$76
16	Pepcid 20mg Tablet	\$ 456,596	6,285	48	\$73
17	Ultram 50mg Tablet	\$ 452,810	10,451	65	\$43
18	Neurontin 300mg Capsule	\$ 391,715	3,714	109	\$105
19	Claritin 10mg Tablet	\$ 389,356	7,016	28	\$55
20	Risperdal 2mg Tablet	\$ 370,083	2,178	50	\$170
21	Depakote 250mg Tablet	\$ 338,551	5,517	87	\$61
22	Rezulin 400mg Tablet	\$ 328,948	2,383	32	\$138
23	Zithromax 250mg Tablet	\$ 303,284	8,111	6	\$37
24	Propulsid 10mg Tablet	\$ 295,669	4,397	99	\$67
25	Lipitor 10mg Tablet	\$ 288,513	5,154	33	\$56