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Indiana Medicaid DUR Board
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Indiana Medicaid Drug Utilization Review Board Newsletter

Practice Guidelines for Treating GERD

Gastric Esophageal Reflux Disease (GERD) is a common, chronic condition caused by the retrograde flow of gastric contents back into the esophagus. Approximately 20% of US adults experience GERD symptoms on a weekly basis. Heartburn, experienced by approximately 10% of the American population daily, is the hallmark symptom. GERD has been shown to have a more profound effect on quality of life than do duodenal ulcers, untreated hypertension, mild congestive heart failure, angina, or menopause.¹

Recently, the Practice Parameters Committee of the American College of Gastroenterology updated their guidelines for the diagnosis and treatment of GERD. The new guidelines are printed in a report found in the June 1999 issue of The American Journal of Gastroenterology.² Treatment guidelines are listed below:

1. Empiric treatment in patients with uncomplicated GERD, initiation of acid suppression agents, and lifestyle modification, are appropriate. Patients who fail empirical therapy, or who

- demonstrate symptoms suggesting complicated disease, should have further diagnostic testing.
2. Lifestyle modification should be initiated and continued throughout the course of GERD therapy. Modifications should include elevating the head of the bed, reducing the patient's dietary fat intake, smoking cessation, and avoiding meals within three hours of sleeping. Certain foods have also been associated with increased esophageal reflux and should be limited, if not avoided altogether. They include chocolate, alcohol, peppermint, coffee, onions and garlic.
3. Acid suppression agents include the proton pump inhibitors (PPIs) and histamine₂-receptor antagonists (H₂-RAs). Utilization of PPIs has demonstrated to provide rapid

First-line treatment of GERD with cisapride is not recommended.

symptomatic relief and healing of esophagitis in the highest percentage of patients with GERD. The legend or non-

- legend H₂-RAs, given in divided doses may also be used and are effective treatment in many patients with less severe symptoms.
4. There are various approaches to the initial treatment of GERD using H₂-RAs and PPIs. The step-up approach starts with a standard or OTC dose of a H₂-RA and titrating to symptom control. The step-down approach starts with once or twice-daily PPI therapy and decreasing the dose in therapy to the lowest form of acid suppression that controls the symptoms. Several studies have concluded that neither approach has been proven superior and therefore which approach to use is best left to the

¹ Fendrick AM, Blitz SG. Gastroesophageal Reflux: Therapy Considerations After Failure of Low-Dose, Nonprescription H₂RAs. Formulary 1999; 34: 234-48.
² Devault KR, Castell DO. Updated Guidelines for the Diagnosis and Treatment of Gastroesophageal Reflux Disease. AJG 1999; 94: 1434-42.

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choice of the prescriber, in consultation with the patient.

- The usefulness of promotility agents such as cisapride and metoclopramide demonstrate an efficacy similar to standard dose H₂-RAs. These agents attempt to correct the central aspects of the pathogenesis of GERD; specifically, those related to lower esophageal sphincter incompetence, poor esophageal clearance, and delayed gastric emptying time. Correcting these defects would control GERD and make the suppression of normal amounts of gastric acid production unnecessary.

The concern with cisapride has been the report of fatal cardiac arrhythmias associated with the combination of cisapride and other drug products that are metabolized by the cytochrome p-450 system. Although cisapride may be useful in certain patients, PPIs provide greater control of acid reflux, without the risk of cardiac rhythm disturbances. **The FDA has issued a warning on cisapride, advising doctors that the drug's use should be intended for patients who have not responded adequately to lifestyle modifications or other drugs for treating symptoms related to GERD. First line treatment of GERD with cisapride is not recommended.**

- GERD should be considered a chronic condition, requiring continuous therapy to control symptoms and preventing complications. Because short- and long-term studies have demonstrated that PPIs have a wide safety margin and a favorable adverse-event profile with few drug interactions,

Antisecretory and Promotility Drugs for Treatment of GERD¹

Drug	Dosage Regimen	Rate of Healing*	Daily Cost*
<i>H₂-receptor antagonists</i>			
Cimetidine		++	
Standard dose	400mg bid		\$3.35
High dose	400mg qid or 800mg bid		\$5.94
Famotidine		++	
Standard dose	20mg bid		\$3.40
High dose	40mg bid		\$6.59
Nizatidine		++	
Standard dose	150mg bid		\$3.20
High dose	150mg qid or 300mg bid		\$6.19
Ranitidine		++	
Standard dose	150mg bid		\$3.44
High dose	150mg qid or 300mg bid		\$6.24
<i>Proton pump inhibitors</i>			
Lansoprazole	15mg qd	+++	\$3.41
Omeprazole	20mg qd	+++	\$3.96
<i>Promotility agents</i>			
Bethanechol	25mg qid	±	\$0.14 (generic)
Cisapride	10-20mg qid	++	\$2.85
Metoclopramide	10-15mg qid	±	\$0.87 (generic)

* ± = limited efficacy or inconsistent results; ++ = 50% to 80%; +++ = > 80%
 * Based on average wholesale price; costs of H₂-RAs are for brand-name versions.

chronic therapy utilizing these products is a safe, effective and appropriate form of maintenance therapy in many of these patients³.

...chronic therapy utilizing these products (PPIs) is a safe, effective and appropriate form of maintenance therapy...

The goals in treating patients with GERD are to eliminate the symptoms, promote mucosal healing, and reduce or prevent complications. Reducing the acidity and volume of the refluxate, and

³ Garnett WR. Considerations for Long-Term Use of Proton-Pump Inhibitors. AJHP 1998; 55: 2268-79.

minimizing the duration in which the refluxate is in contact with the mucosa, typically leads to the best outcomes¹.

Counseling patients on lifestyle modifications should be conducted on all patients, regardless of their severity. Certain medications that are commonly prescribed such as calcium channel blockers, narcotic agents, and estrogens may worsen reflux and alternative therapies should be considered, if feasible¹.

The table above is a listing of the recommended dosing regimens, relative effectiveness, and costs associated with commonly prescribed drug products used in the treatment of GERD. Although antacids were not included in this table, they are often used concurrently with the prescription antisecretory agents when complete symptom relief is not achieved.

Visit the Indiana Medicaid DUR Board website at www.indianamedicaid.com

Review of Prospective Drug Utilization Alerts from June 1999 Pharmacy Claims

A review of Pro-DUR alerts for June 1999 revealed 623 drug/drug interaction alerts issued involving claims for fluoroquinolones. There is substantial evidence concerning the interference that antacids, iron and zinc salts have on the GI absorption of fluoroquinolones, resulting in decreased serum levels and potential treatment failures. Nearly 72% of these alerts were overridden and dispensed. The Board reminds pharmacists of the advisability of counseling patients about the use of antacids and vitamin supplements containing iron and zinc when dispensing fluoroquinolone prescriptions.

A review of therapeutic duplication alerts from June’s Pro-DUR Report revealed occurrences involving benzodiazepines, Selective Serotonin Reuptake Inhibitors (SSRIs), and H₂-Antagonists. There were 1873 therapeutic duplication alerts involving benzodiazepines in which 1406 of those alerts were overridden by the pharmacist. Alerts involving therapeutic duplications of SSRIs totaled 1757, with 1419 overrides. Finally, 186 alerts were generated from therapeutic duplications of H₂-Antagonists; 154 of those alerts were overridden. The DUR Board encourages pharmacists receiving therapeutic duplication alerts when submitting claims, to contact the prescriber when appropriate to determine if one of the agents can be discontinued.

The Pro-DUR Program

The purpose of the Prospective Drug Utilization Review (Pro-DUR) Program with Indiana Medicaid is to improve the quality and cost effectiveness of drug use by ensuring that prescriptions are appropriate, medically necessary, and not likely to result in adverse medical events. “Appropriate and medically necessary” refers to drug prescribing and dispensing that conforms to predetermined criteria and standards

Pro-DUR Alerts (June 1999 Claims)

Drug Products	Alerts	Overrides
Drug/Drug Interactions (DD) with Fluoroquinolones - from 2380 total claims With ciprofloxacin - 540 alerts With ofloxacin – 50 alerts With norfloxacin – 31 alerts With grepafloxacin – 1 alert With lomefloxacin – 1 alert	623	446
Therapeutic Duplications (TD) with Benzodiazepines	1873	1406
Therapeutic Duplications (TD) with SSRIs	1757	1419
Therapeutic Duplications (TD) with H₂-Antagonists	186	154

established by the Indiana Medicaid DUR Board.

Indiana Medicaid currently screens for eight Pro-DUR alerts. These alerts are Drug/Pregnancy (PG), High Dose (HD), Drug/Age-Pediatric (PA), Drug /Drug (DD), Therapeutic Duplication (TD), Underutilization (LR), Overutilization (ER), and Drug/Disease (MC). Within each of these alerts are specific drugs or therapeutic classes of drugs that are screened to determine if an alert will be set. These drugs and therapeutic classes are received from First DataBank and are updated on a monthly basis in the IndianaAIM POS system. All clinical criteria from First DataBank are according to FDA labeling and current medical and pharmacy literature. The DUR Board reviews and approves all updated criteria that are activated in the IndianaAIM POS system. The following information describes the Pro-DUR alerts that pharmacists may come across when submitting drug claims to Indiana Medicaid through the POS system:

Drug/Pregnancy Alert (PG)

The Drug/Pregnancy alert is set if the drug is inappropriate for use during pregnancy, according to FDA-assigned

pregnancy risk categories. IndianaAIM screens for this alert if the pharmacist indicates on the claim that the recipient is pregnant. If the pharmacist inadvertently indicates that a small child, a male, or a geriatric recipient is pregnant they could receive this alert. *Just removing the pregnancy indicator will not get the claim to pay if the pregnancy alert is set. The pharmacist must respond to the alert.*

High Dose Alert (HD)

A High Dose alert is set if the dosage lies outside the usual adult daily dosage range based on predetermined criteria and standards.

Drug/Age-Pediatric (PA)

The Drug/Age-Pediatric alert is set if the drug is inappropriate for use in patients under the age of eighteen.

Overutilization Alert (ER)

The Overutilization alert is set if the drug is used in quantities or for a duration that places the patient at risk of an adverse medical event. *The DUR Board has determined that a recipient may request a refill within five days of the next refill before the overutilization alert will be set.*

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Underutilization Alert (LR)

The underutilization alert is set when a drug is used in an insufficient quantity to achieve a desired therapeutic goal.

Drug/Drug Alert (DD)

The Drug/Drug alert is set when the use of two or more drugs will create a different pharmacological or pharmacokinetic response than is expected when the drugs are given separately and creates the potential for an adverse medical event.

Therapeutic Duplication Alert (TD)

The Therapeutic Duplication alert is set when two or more drugs are received from the same therapeutic or pharmacologic class and the combined daily dose increases the risk of an adverse medical event or incurs additional program costs without additional therapeutic benefit.

Drug/Disease Alert (MC)

The Drug/Disease alert is set when a drug is contraindicated for use with patients of specific disease states, as inferred from the drug therapy reported in their pharmacy profiles.

Top 25 Drugs By The Total Dollars Paid in First Quarter 1999

The top 25 drug products based on the total dollars spent for first quarter 1999, represented \$16,935,278 in Indiana Medicaid payments to pharmacy providers. Antipsychotic agents topped the list with 6 products attributing to \$4,594,320 in Medicaid payments. Gastrointestinal agents and Selective Serotonin Reuptake Inhibitors represented 4 products each, with Medicaid payment amounts of \$4,246,283 and \$2,734,026, respectively. Anticonvulsant agents were the last group of products representing 3 products and \$1,479,252 in Medicaid payments.

Drug Product	Total Claims	Quantity Dispensed	Total Payment
1. Prilosec 20mg Capsule	18,038	646,785 Caps	\$2,253,195
2. Zyprexa 10mg Tablet	6,333	280,228 Tabs	\$2,055,646
3. Prozac 20mg Pulvule	12,600	560,003 Caps	\$1,259,752
4. Prevacid 30mg Capsule	9,349	324,941 Caps	\$1,051,237
5. Recombinate 801-1240	136	981,119 U	\$985,453
6. Depakote 500mg Tab EC	6,507	558,993 Tabs	\$706,284
7. Risperdal 1mg Tablet	6,862	297,405 Tabs	\$641,052
8. Synagis 100mg Vial	379	546 ml	\$588,208
9. Zyprexa 5mg Tablet	2,892	111,356 Tabs	\$545,339
10. Risperdal 3mg Tablet	2,336	122,921 Tabs	\$509,989
11. Zolof 50mg Tablet	7,077	247,403 Tabs	\$506,094
12. Axid 150mg Pulvule	6,605	344,028 Caps	\$503,714
13. Zolof 100mg Tablet	6,458	242,412 Tabs	\$499,164
14. Paxil 20mg Tablet	6,618	233,466 Tabs	\$469,016
15. Clozaril 100mg Tablet	3,136	151,620 Tabs	\$465,706
16. Ultram 50mg Tablet	10,201	670,326 Tabs	\$460,206
17. Benefix 1000IU Vial	70	536,566 U	\$448,711
18. Pepcid 20mg Tablet	5,925	287,639 Tabs	\$438,137
19. Neurontin 300mg Cap	3,943	435,282 Caps	\$420,582
20. Claritin 10mg Tablet	7,062	106,715 Tabs	\$371,772
21. Risperdal 2mg Tablet	2,152	106,715 Tabs	\$376,588
22. Zithromax 250mg Z-Pak	9,842	59,681 Tabs	\$369,930
23. Depakote 250mg Tab EC	5,653	499,429 Tabs	\$352,386
24. Rezulin 400mg Tablet	2,278	75,366 Tabs	\$321,397
25. Lipitor 10mg Tablet	5,564	183,274 Tabs	\$316,020

DUR Board Calendar

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

FDA WARNINGS

The FDA issued a public health advisory to physicians concerning the risks of liver toxicity associated with the use of **Trovan**[®] (trovafloxacin) and **Trovan**[®] **IV** (atrovafloxacin). This action follows postmarketing reports of rare but severe liver injuries leading to transplants and deaths. Pfizer Inc. will be notifying physicians to limit the use of **Trovan**[®] to certain serious infections.

The FDA is advising physicians about new safety concerns regarding the use of **Enbrel**[®] (etanercept). Postmarketing reports indicate that certain patients receiving **Enbrel**[®] have developed serious infections, including sepsis, and that several of these patients have died from their infections.