

OREGON DUR BOARD NEWSLETTER[©]

AN EVIDENCE BASED DRUG THERAPY RESOURCE

© COPYRIGHT 2003 OREGON STATE UNIVERSITY. ALL RIGHTS RESERVED

Volume 5, Issue 7

Also available on the web and via e-mail list-serve at

September 2003

http://pharmacy.oregonstate.edu/drug_policy/newsletter_email.htm

The OHP Preferred Drug List: What is it, what's on it and why?

By Kathy L. Ketchum, R.Ph., MPA:HA, OSU College of Pharmacy

The Oregon Health Plan (OHP) Practitioner-Managed Prescription Drug Plan (PMPDP) or plan drug list (PDL) has garnered national recognition for its reliance on clinical evidence but remains unclear to many Oregon physicians, pharmacists and other clinicians serving open-card OHP patients.^{1 2 3 4} This article will briefly review the history of the PMPDP, review the most recent evidence evaluations and identify preferred products.

The Health Resources Commission (HRC) was charged with recommending drugs from selected classes that represent the most effective and safe drugs for the majority of OHP patients. The advice is crafted using peer-reviewed literature and applying established evidence-based methods. It is developed with the assistance of the Oregon Health Sciences University Evidence-Based Practice Center (EPC) and HRC subcommittees of volunteer health care providers and consumer representatives. The evaluations are done in a public forum and are made freely available.⁵ Once a drug or group of drugs is determined by the HRC to be of superior or comparable effectiveness and safety, the Office of Medical Assistance Programs (OMAP) determines which of the drugs are least costly for the State and lists them at www.oregonrx.org.

The PDL was envisioned as a guide for OHP clinicians to identify cost-effective drug selections. However, in January 2003 under the crunch of a collapsing State budget and imminent enrollment reductions, OMAP staff evaluated the impact of this passive approach and found it to be inadequate to meet the budget goals of the legislation. Beginning February 2003, OHP open-card patients were required to pay differential co-pays for branded products. On May 2003, prescribers of non-PDL drugs for open-card patients were required to actively request an exception to the PDL by calling the State's contractor (800-344-9180). Figure 1 demonstrates the financial impact of these policy changes on the four initial PDL drug classes. The 2003 legislature prohibited the agency from the requiring request exceptions and beginning October 1, 2003 the PDL becomes voluntary again.

and are an applied, local interpretation of the more extensive EPC reports. Both reports are found at www.oregonrx.org. A brief synopsis of each HRC report is provided below.

ESTROGENS

The HRC Estrogen Report was released January 2003.⁷ It summarizes the subcommittee's evaluation of the comparative effectiveness and safety of various estrogen products in oral, vaginal and transdermal forms. It focused on the effectiveness in peri- and post-menopausal women for the treatment of menopausal symptoms and for the prevention of osteoporosis. The subcommittee evaluated the comparative safety of estrogen preparations in the same population for short-term use and long-term use.

The subcommittee concluded that all estrogen preparations reduced hot flashes, sleep disturbances, mood changes and urogenital symptoms. Studies measuring sexual dysfunction and quality of life were inadequate to determine any clinical relevance. All estrogen preparations improve bone density and some studies demonstrate a dose-response effect. Estrogen use reduces fractures. Most studies are of estradiol and conjugated equine estrogen. For other estrogen preparations, clinical trials are few and evidence cannot establish clinically significant differences or equality.

The evidence suggested that serious and nuisance side effects can be associated with hormone therapy but there were no comparison studies between estrogen products. The data was inadequate to evaluate effects of dose and of the role of progestins/progesterone.

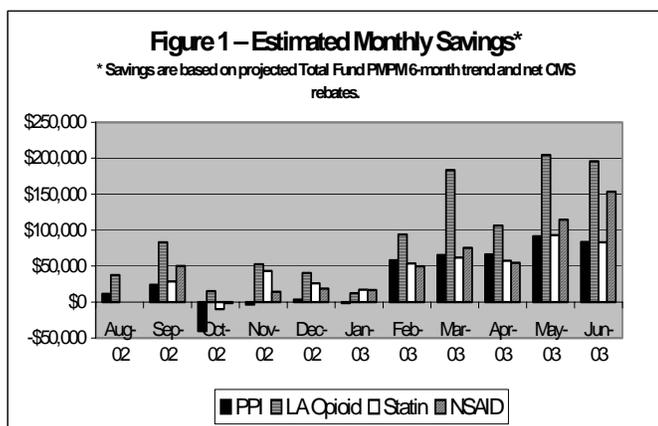
The evidence did not identify subgroups of patients for which one medication or preparation is more effective or associated with fewer side effects. Women's Health Initiative data regarding racial and ethnic groups are anticipated to become available as the findings continue to be analyzed.

TRIPTANS

The HRC Triptan Report was released March 2003.⁸ The subcommittee focused on oral triptans and did not review the fast dissolving products due to the lack of comparison data. Eletriptan and Frovatriptan were not considered because of the lack of available peer-reviewed data.

The subcommittee evaluated oral triptans for migraine as defined by the International Headache Society. The subcommittee primarily reviewed effectiveness based on 2-hour pain relief, 2-hour pain free and 24-hour pain relief. The criteria were selected based upon what many studies identified as important to migraine sufferers; prompt relief above all else. Using the criteria, oral rizatriptan appeared to be the most effective. However, the clinical relevance of rizatriptan's superiority was not elucidated by the committee. There was sufficient evidence to also recommend sumatriptan and zolmitriptan for the initial therapy for migraine patients.

The subcommittee found that patient surveys indicate that migraineurs are willing to endure significant side effects to achieve pain relief and side effects are not a determining factor in choosing a triptan. Important differences between equivalent doses of triptans with regard to adverse events were not found. There are clear medical contraindications to the use of triptans, with no difference evidenced between them. Triptans are effective in treating menstrual-induced migraine. There is no comparative evidence to assess differences in effectiveness and safety in patients of differing race, ethnic group, age or gender.



The first four classes were reviewed in a previous issue.⁶ The preferred drug options are listed in Table 1. The benchmark drug represents the best value and establishes the price bar for other drugs in the class.

The HRC has recently completed reviews for the estrogens, triptans, urinary incontinence drugs, skeletal muscle relaxants and oral hypoglycemics. The HRC reports are a product of extensive public debate by the subcommittees

URINARY INCONTINENCE DRUGS

The HRC Urinary Incontinence Drug Report was released April 2003.⁹ The subcommittee evaluated flavoxate, oxybutynin and tolterodine (both immediate release and long-acting formulations) for adult patients with symptoms of urge incontinence/overactive bladder.

The subcommittee found that overall, the available evidence did not demonstrate significant differences in objective or subjective effectiveness measures among any comparisons of oxybutynin IR, oxybutynin ER, tolterodine IR and tolterodine ER. At present there is no evidence demonstrating the effectiveness of flavoxate.

The subcommittee also found that overall, available evidence does not demonstrate significant differences in adverse events or withdrawal effects among oxybutynin and tolterodine or among immediate release and extended release forms of these medications. There was insufficient evidence to draw conclusions about the comparative effectiveness or safety of incontinence drugs on subgroups.

SKELETAL MUSCLE RELAXANTS

The HRC Skeletal Muscle Relaxant Report was released April 2003.¹⁰ The subcommittee recognized that the skeletal muscle relaxants are a heterogeneous group of medications that are commonly used to treat two different types of underlying conditions: spasticity from upper motor neuron syndromes and muscular pain or spasms from peripheral musculoskeletal conditions. Although these drugs have been classified into one class, the Food and Drug Administration (FDA) has approved only baclofen, dantrolene, and tizanidine in this class for the treatment of spasticity; tizanidine and the remainder of the skeletal muscle relaxant class are approved for treatment of musculoskeletal conditions. Benzodiazepines were included as comparators but could not be formally included due to statutory prohibition.

The subcommittee found that the evidence does not distinguish a difference in effectiveness between baclofen, dantrolene or tizanidine for spasticity associated with chronic neurological conditions. Nearly all the studies for musculoskeletal conditions were limited to short-term treatment and showed only a modest clinical effect. Cyclobenzaprine had the largest body of evidence to support its efficacy. Metaxalone was shown to be not effective.

The subcommittee concluded that evidence suggested there are different nuisance side effect profiles associated with baclofen, dantrolene, or tizanidine. Dantrolene is associated with rare but fatal hepatotoxicity and tizanidine requires monitoring of liver function tests as it may also pose a risk for hepatotoxicity. The evidence does not support any conclusions about the comparative safety of any of the skeletal muscle relaxants in patients with musculoskeletal conditions. No conclusions could be drawn regarding the comparative effectiveness or adverse effects for different subpopulations of patients such as race, gender, or age.

ORAL HYPOGLYCEMICS

The Oral Hypoglycemic Report was released April 2003.¹¹ The subcommittee evaluated the comparative effectiveness of sulfonylureas and the short-acting secretagogues; repaglinide and nateglinide in adult patients with Type 2 diabetes. Effectiveness was measured by the ability to lower HbA1c and with long-term outcomes such as: time to insulin, progression/occurrence of microvascular disease, progression/occurrence of macrovascular disease, complications of diabetes, all-cause mortality and quality of life.

The subcommittee found that for all the agents in these two classes current evidence shows no clinically significant difference between any of these agents in ability to lower HbA1c. They found that there is no statistically significant difference between glyburide and chlorpropamide in progression or occurrence of clinically relevant outcomes with the exception of retinopathy. Patients on glyburide had greater risk reduction of progression of retinopathy than those on chlorpropamide. There is insufficient evidence to comment on other sulfonylureas and nonsulfonylureas secretagogues.

The subcommittee found that chlorpropamide has a less favorable adverse effect profile compared to glyburide. Glimperide, glipizide, glyburide,

micronized glyburide and repaglinide do not differ in safety or adverse effect profile. No evidence exists for the comparative safety evaluation of tolbutamide, tolazamide or nateglinide.

The subcommittee found that among the demographic subgroups including obesity, currently available evidence does not suggest that any one oral hypoglycemic agent is more effective or associated with fewer adverse effects than any other oral hypoglycemic agent. Evidence is lacking in comparative effectiveness and side effects of these agents in the subgroups with concomitant medications, other co-morbidities besides obesity, or history of hypoglycemic episodes.

CONCLUSION

The OHP PDL saved approximately \$500,000 per month in drug costs using a phone call for exceptions. It is nationally recognized for its reliance on clinical evidence for drug selection decisions but remains unclear to many Oregon providers. Extensive public debate by local, volunteer clinicians help to interpret and apply practical experience to structured evidence reviews. All background information and drug selections are available at WWW.OREGONRX.ORG. Clinicians who would like to participate on a subcommittee are encouraged to contact Betty Wilton at [BETTY.WILTON@STATE.OR.US](mailto: BETTY.WILTON@STATE.OR.US) or 503-378-2422.

Table 1 – PMPDP Preferred Drugs Effective November 1, 2003

	Benchmark Drug	Other options
Long-Acting Opioid Analgesics	long-acting morphine (generic)	Oramorph SR Kadian methadone (generic) levorphanol (generic)
Proton Pump Inhibitors	Protonix	Aciphex Prevacid
HMG-CoA Reductase Inhibitors (Statins)	lovastatin (generic)	Pravachol
NSAIDs (includes COXII & COXII preferential drugs)	naproxen (generic)	ibuprofen (generic) piroxicam (generic)
Estrogens	oral estradiol (generic)	Ogen, Activella, Ortho-Est, Cenestin, Premarin (oral), Estrace (oral), Premphase, Estropipate, Prempro, Femhrt, Menest
Triptans	Maxalt	Zomig Imitrex (all forms)
Urinary Incontinence Drugs	oxybutynin IR (generic)	
Skeletal Muscle Relaxants	baclofen (generic) cyclobenzaprine (generic)	
Oral Hypoglycemics	glyburide (generic)	glipizide (generic)

REFERENCES

- Cain B; "Physicians not supporting cost-saving rule", The Eugene Register Guard, July 14, 2003.
- Palfreman P, Moran B; PBS Frontline "The Other Drug War"; aired June 19, 2003, available at www.pbs.org.
- "Oregon Drug Plan Draws National Attention", The Oregonian, October 10, 2002.
- Winslow R, McGinley L, Adams C; "States, Insurers Find Solutions for Drug Costs", The Wall Street Journal: September 11, 2002.
- Oregon's Practitioner-Managed Prescription Drug Plan: Evidence Based Information on Prescription Drugs for Consumers and Health Care Providers. www.oregonrx.org.
- Ketchum K; "HRC Reports Evidence in First Classes for OHP Drug Plan", Oregon DUR Board Newsletter: V4:14 June 2002. Available at: pharmacy.oregonstate.edu/drug_policy/news/4_4_4_4.html.
- Estrogen For Treatment of Menopausal Symptoms and Prevention of Low Bone Density & Fractures; Oregon Health Resources Commission. January 2003. Available at: www.oregonrx.org.
- Triplan; Oregon Health Resources Commission. March 2003. Available at: www.oregonrx.org.
- Urinary Incontinence; Oregon Health Resources Commission. April 2003. Available at: www.oregonrx.org.
- Skeletal Muscle Relaxants; Oregon Health Resources Commission. April 2003. Available at: www.oregonrx.org.
- Oral Hypoglycemics; Oregon Health Resources Commission. April 2003. Available at: www.oregonrx.org.

