

Wyoming Drug Utilization Review



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New Medications and Multiple Antidepressant Use in Depression

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New Antidepressants

The development of new antidepressant agents is an important area of need in the medical field. New agents expand the expected therapeutic effect and tolerability of antidepressant therapy.¹ Two new antidepressants have been approved for marketing this year, duloxetine and escitalopram. It is imperative for clinicians to research the new medications being approved, to be able to fully understand their place in therapy.

Duloxetine is a dual reuptake inhibitor of serotonin and norepinephrine. This medication lacks significant affinity for muscarinic, histaminergic, adrenergic, dopaminergic and opioid receptors, thus resulting in a decreased incidence of adverse events.¹ Duloxetine offers the potential to test the hypothesis that a dual-reuptake inhibitor will have a greater antidepressant effect than a medication with only single reuptake inhibition (i.e. SSRIs). Sexual dysfunction, vital signs and body weight were specifically looked at during a study with duloxetine and there were no statistically significant differences found between the duloxetine- and placebo-treated groups.¹ This study confirms the data suggesting that duloxetine may potentially be an important advancement in the treatment of patients with major depression.

Escitalopram (Lexapro®) is the active S-enantiomer of racemic citalopram (Celexa®), a selective serotonin reuptake inhibitor (SSRI). It has been shown to be twice as potent as the racemic mixture.² A couple of studies were performed comparing escitalopram 10mg to citalopram 20mg and 40mg and placebo. The studies found escitalopram 10mg and citalopram 40mg had similar effects on decreasing depression rates in patients and these effects were statistically significant when compared to the effects of citalopram 20mg and placebo.² Although escitalopram has been found to be an effective treatment for depression it has not been shown to be more effective, quicker acting, or less likely to cause adverse events (including sexual

dysfunction), than citalopram or any other SSRIs or antidepressants.

Multiple Antidepressant Use

A review of literature concerning the use of multiple antidepressants is very limited. The inherent limitations of small sample size and nonrandomized design of current available studies lead us to conclude that larger, randomized trials are needed to examine the benefits (i.e. suggest better outcomes and/or efficacy) and risks of combination antidepressant therapies.³

References:

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Coenzyme Q10 and the HMG-CoA Reductase Inhibitors

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As its name implies, ubiquinone (or coenzyme Q10) is found in every cell in the body, and is fundamental for energy production by the cell. Ubiquinone was identified in 1958, and subsequent research demonstrated its essential role in oxidative phosphorylation (ATP production) in mitochondria. CoQ10 is also an antioxidant and membrane stabilizer, and is structurally similar to vitamin K. It is found naturally in fish and fish oil, organ meats, and the germ of whole grains. In vivo biosynthesis of CoQ10 occurs from the amino acid tyrosine in the presence of adequate levels of folic acid, niacin, pyridoxine, and riboflavin.

CoQ10 deficiency may occur with environmental stress, strenuous exercise, inadequate dietary intake, and with selected drugs. Reports of deficiency also exist for some disease states, e.g.; AIDS, cancer, cardiomyopathy, chronic obstructive pulmonary disease, congestive heart failure, hypertension, and periodontal disease. CoQ10 has been used therapeutically in all of the disease states mentioned above. In Japan, millions of patients have used CoQ10 for cardiovascular disease since its approval in 1974. CoQ10 is also widely used in the United States and Europe.¹

Ubiquinone is a fat-soluble isoprenoid and is “down-stream” of the HMG-CoA reductase enzyme in the biochemical pathway of cholesterol synthesis; it is also a lipophilic component of low-density lipoprotein. Intuitively, then, it is proposed that treatment with drugs that inhibit this enzyme, i.e., the “statins” will lead to a decrease in the level of ubiquinone in the body. It follows that supplementation with CoQ10 may be beneficial in maintaining normal cellular respiration and possibly preventing statin-induced myopathy.²

As is the case with many dietary supplements, quality (randomized, double-blind, placebo-controlled) research studies are difficult to find. In addition, research studies that are available often offer conflicting conclusions. A recent randomized crossover trial as well as one other previously published study found no decrease in circulating CoQ10 in patients using statins.²⁻³ Contrarily, two older studies indicated a dose-related decrease in serum ubiquinone in patients treated with various statins.⁴⁻⁵

It should be noted that a surrogate outcome is used in these studies, i.e., serum ubiquinone level. Because statin-induced myopathy is a rare event, designing a research protocol for this outcome would require an extremely large sample size to detect any significant effect. In addition, the majority of patients using statins are treated on a long-term

basis, and the effect of possible long-term CoQ10 depletion remains unaddressed.

Adverse effects documented with CoQ10 include epigastric discomfort, appetite suppression, nausea, and diarrhea. However, these are minor. Patients and practitioners should be aware that ubiquinone might decrease the effectiveness of warfarin due to structural similarities between ubiquinone and vitamin K. Doses exceeding 300 mg/day have been associated with an increase in serum liver enzymes. The normal dose recommended to prevent deficiency is approximately 1 mg/kg, or 30-60 mg/day. Therapeutic doses of 100-200 mg/day are recommended for patients with heart disease. Doses exceeding 100 mg should be divided.²

CoQ10 is available in a wide range of oral and topical forms, that range in price from less than ten to approximately sixty dollars per month, depending on dosage.⁶ When one considers the expense of a monthly statin prescription, routinely recommending CoQ10 would be a significant additional monthly expense.

In conclusion, although coenzyme Q10 is widely recommended and used in industrialized countries, there is a lack of quality research to demonstrate its effectiveness. Nevertheless, because it is so widely used, it is known that CoQ10 is relatively safe and may be beneficial for some patients, especially those with chronic heart disease. Further studies are needed to confirm the efficacy of CoQ10 in patients with heart disease and other chronic illness. Routine supplementation in otherwise healthy patients taking statins does not seem to be a cost-effective treatment at this time. For sicker patients with chronic illness who are interested in CoQ10 supplementation, practitioners should discuss the possible benefits and cost of treatment with the patient.

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Top 50 Prescriptions by Dollar Total Wyoming Medicaid 2002

	DRUG	Rx Count	Dollar Total
1	ZYPREXA (olanzapine)	7348	\$2,015,102
2	PRILOSEC (omeprazole)	6075	\$962,365
3	RISPERDAL (risperidone)	5539	\$959,718
4	PREVACID (lansoprazole)	6862	\$927,169
5	SEROQUEL (quetiapine)	5458	\$903,208
6	ZOLOFT (sertraline)	10133	\$800,508
7	NEURONTIN (gabapentin)	6159	\$781,068
8	DEPAKOTE (divalproex)	6495	\$753,986
9	PAXIL (paroxetine)	7254	\$617,386
10	CELEXA (citalopram hydrobromide)	7967	\$583,331
11	CLARITIN (loratadine)	6640	\$550,318
12	ZITHROMAX (azithromycin)	12380	\$471,132
13	WELLBUTRIN (bupropion)	5065	\$468,382
14	EFFEXOR (venlafaxine)	4539	\$463,112
15	CELEBREX (celecoxib)	4391	\$439,060
16	VIOXX (rofecoxib)	5211	\$431,787
17	LAMICTAL (lamotrigine)	1723	\$408,588
18	DURAGESIC PATCH	2345	\$407,259
19	AVONEX (interferon beta-1a)	436	\$397,019
20	OXYCONTIN (oxycodone)	2558	\$377,833
21	SINGULAIR (montelukast)	4484	\$372,661
22	CONCERTA (methylphenidate)	4720	\$362,334
23	MONONINE (antihemophilic Factor IX complex)	6	\$355,129
24	AUGMENTIN (amoxicillin)	4488	\$336,582
25	SYNAGIS (palivizumab)	281	\$331,904

	DRUG	Rx Count	Dollar Total
26	ADVAIR (salmeterol)	2589	\$319,932
27	NEXIUM (esomeprazole magnesium)	2462	\$308,530
28	LIPITOR (atorvastatin)	3520	\$306,629
29	RECOMBINATE (antihemophilic Factor VIII recom)	16	\$275,381
30	ADDERALL (amphet asp)	3380	\$271,300
31	TOPAMAX (topiramate)	1337	\$264,846
32	CLOZARIL (clozapine)	1395	\$261,376
33	COPAXONE INJECTION KIT	234	\$260,262
34	ZYRTEC (cetirizine)	4695	\$240,482
35	TRILEPTAL (oxcarbazepine)	1439	\$233,390
36	PROTONIX (pantoprazole)	2223	\$215,569
37	FLUOXETINE	2376	\$194,436
38	AVANDIA (rosiglitazone maleate)	1608	\$193,416
39	REMERON (mirtazapine)	2209	\$178,986
40	DETROL (tolterodine tartrate)	2097	\$175,654
41	NOVOSEVEN (antihemophilic Factor VIIa recom)	8	\$169,460
42	LEVAQUIN (levofloxacin)	2231	\$163,682
43	PLAVIX (clopidogrel bisulfate)	1400	\$155,437
44	DITROPAN (oxybutynin)	1861	\$152,119
45	NORVASC (amlodipine)	2648	\$149,976
46	GEODON (ziprasidone)	697	\$145,730
47	FLOVENT INHALER	1545	\$138,888
48	ENBREL (etanercept)	118	\$137,908
49	ACIPHEX (rabeprazole)	1069	\$135,382
50	FOSAMAX (alendronate)	1996	\$131,829

Prior Authorization Savings Wyoming Medicaid

DRUG	Oct-02	Nov-02	Dec-02	Jan-03	Feb-03	Mar-03	Total Savings
COX II	\$45,853	\$45,032	\$37,010	\$30,598	\$46,063	\$44,960	\$249,516
PPI	\$72,007	\$59,863	\$71,505	\$59,466	\$107,410	\$111,645	\$481,896
Total Savings Net of Administrative Costs	\$97,692	\$94,431	\$99,615	\$81,549	\$146,675	\$151,057	\$671,019

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