

Bon Secours Richmond  
Pharmacy and Therapeutics Committees  
Paxil CR  
11/2004

Recommendations: P&T/MEC approved all sites

- Paxil CR and paroxetine immediate release are equally effective and tolerable; generic paroxetine will be autosubstituted for Paxil CR at the equivalent dose (80% of the Paxil CR Dose).
- Each dose of paroxetine substituted for Paxil or Paxil CR will result in average savings of 25%.

Findings:

- Paxil's patent has recently expired and generic paroxetine is available at a lower cost.
- Paxil CR is a patented product by GlaxoSmithKline the maker of Paxil.
- Paxil CR is an enteric, film-coated tablet embedded in a hydrophilic matrix. Due to incomplete dissolution from the matrix, the dose of Paxil CR is 25% higher than the dose of Paxil.
- Discontinuation rates due to nausea for Paxil CR and Paxil are similar 3.7% and 3.2% respectively.

<b>FDA Approved Indications</b>		
	Paxil	Paxil CR
Major Depressive Disorder	Initial: 20 mg/day Maintenance: 20-50 mg/day	Initial: 25 mg/day Maintenance: 25-62.5 mg/day
Obsessive Compulsive Disorder	Initial: 20 mg/day maintenance: 40 mg/day	Not indicated
Panic Disorder	Initial: 10 mg/day Maintenance: 40 mg/day	Initial: 12.5 mg/day Maintenance: 12.5-75 mg/day
Social Anxiety Disorder	Initial: 20 mg/day Maintenance: 20-60 mg/day	Initial: 12.5 mg/day Maintenance: 12.5-37.5 mg/day
Generalized Anxiety Disorder	Initial: 20 mg/day Maintenance: 20-50 mg/day	Not indicated
Postramatic Stress Disorder	Initial: 20 mg/day Maintenance: 20-50 mg/day	Not indicated
Premenstrual Dysphoric Disorder	Not indicated	Initial: 12.5 mg/day Maintenance: 12.5-25 mg/day

<b>Dosage Equivalence Table</b>			
Ordered	mg	Substitute	mg
Paxil CR	12.5	Paroxetine	10
Paxil CR	25	Paroxetine	20
Paxil CR	37.5	Paroxetine	30
Paxil CR	50	Paroxetine	40
Paxil CR	62.5	Paroxetine	50
Paxil CR	75	Paroxetine	60

**Paxil and Paxil CR ordered from 08/01/2003-07/31/2004**

<b>Item</b>	<b>Cost/ dose</b>	<b>MRMC</b>	<b>RCH</b>	<b>SMH</b>	<b>Total doses</b>	<b>Total cost</b>	<b>Cost of Equivalent Dose of Paroxetine</b>	<b>Yearly Cost Saving</b>
Paroxetine 10 mg	\$1.70	0	0	0	0	\$0.00		
Paroxetine 20 mg	\$1.72	0	0	0	0	\$0.00		
Paroxetine 30 mg	\$1.82	0	0	0	0	\$0.00		
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Paxil 10mg	\$2.24	0	0	29	870	\$1,949.96	\$1,475.43	\$474.53
Paxil 20 mg	\$2.39	22	15	21	5800	\$13,845.18	\$10,002.68	\$3,842.50
Paxil 30 mg	\$2.41	0	0	8	240	\$578.32	\$437.21	\$141.11
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Paxil CR 12.5	\$2.20	17	14	21	1560	\$3,425.76	\$2,645.60	\$780.16
Paxil CR 25	\$2.29	16	18	32	1980	\$4,537.50	\$3,414.71	\$1,122.79
Paxil CR 37.5	\$2.36	0	0	0	0	\$0.00	\$0.00	\$0.00
<b>Total</b>					<b>10450</b>	<b>\$24,336.72</b>	<b>\$17,975.63</b>	<b>\$6,361.09</b>

- Converting all Paxil and Paxil CR to Paroxetine would save \$6,361.09 per year.
- Paroxetine is 25% cheaper than Paxil and Paxil CR per dose.

**Contraindications:**

- Concomitant use in patients taking either monoamine oxidase inhibitors (MAOIs) or thioridazine contraindicated (see WARNINGS and PRECAUTIONS).
- Paxil and Paxil CR are contraindicated in patients with a hypersensitivity to paroxetine or any of the inactive ingredients.

Studies:

**Efficacy and tolerability of controlled-release and immediate-release paroxetine in the treatment of depression.**

Golden RN - *J Clin Psychiatry* - 01-JUL-2002; 63(7): 577-84

**Abstract:**

**BACKGROUND:** Antidepressant efficacy may be compromised by early discontinuation of treatment secondary to common, treatment-emergent side effects, including nausea, agitation, and somnolence. Paroxetine controlled-release (CR) was developed to improve general tolerability and, in particular, gastrointestinal tolerability.

*NOTE: This study was not prospectively designed to compare active treatments with each other, but rather was powered to compare active treatments groups with placebo*

**OBJECTIVE:** To determine the antidepressant efficacy and tolerability of paroxetine CR in adult patients 18 to 65 years of age with DSM-IV major depressive disorder.

**METHOD:** Paroxetine CR (25-62.5 mg/day; N = 212) and paroxetine immediate-release (IR; 20-50 mg/day; N = 217) were compared with placebo (N = 211) in the pooled dataset from 2 identical, double-blind, 12-week clinical trials.

**RESULTS:** Both paroxetine CR and paroxetine IR exhibited efficacy in major depressive disorder as assessed by the reduction in 17-item Hamilton Rating Scale for Depression total score compared with placebo. Moreover, depressed mood and psychic anxiety symptoms improved as early as treatment week 1 in the paroxetine CR group compared with the placebo group. After 6 weeks of treatment, response and remission rates were 41.5% and 20.5% for placebo, 52.8% and 29.6% for paroxetine IR, and 58.9% and 34.4% for paroxetine CR, respectively. After 12 weeks of treatment, response and remission rates were 61.2% and 44.0% for placebo, 72.9% and 52.5% for paroxetine IR, and 73.7% and 56.2% for paroxetine CR, respectively. Rates of nausea were significantly lower for paroxetine CR (14%) than for paroxetine IR (23%;  $p < \text{or} = .05$ ) during week 1, however, by week 3, the rates of nausea between the two groups were equal (approximately 8%). By week 4, Paxil CR had a higher incidence of nausea than Paxil IR (4% vs 2%). Drop out due to adverse events were comparable between Paxil CR and Paroxetine immediate release.

**CONCLUSION:** Paroxetine CR and Paroxetine IR are both equally effective antidepressants exhibiting symptomatic improvement as early as week 1. Paroxetine CR and Paroxetine IR have statistically significant higher rates of nausea than placebo during week one of therapy. The rate drops during continuation of therapy and is comparable to placebo. Dropout rates due to adverse events comparable for Paxil CR and Paroxetine IR.

**Efficacy of controlled-release paroxetine in the treatment of late-life depression.**

Rapaport MH - *J Clin Psychiatry* - 01-SEP-2003; 64(9): 1065-74

**BACKGROUND:** Depression is the second most common neuropsychiatric disorder in older Americans, with significant clinical and public health costs. Despite advances in treatment, late-life depression remains a clinical challenge. Although the selective serotonin reuptake inhibitors (SSRIs) are the most common pharmacologic intervention for late-life depression, few placebo-controlled trials have assessed the efficacy of SSRIs for this condition.

**METHOD:** In this 12-week, multicenter, placebo-controlled, flexible-dose, double-blind, randomized trial, 319 elderly patients (mean age = 70 years) were treated with controlled-release paroxetine (paroxetine CR) up to 50 mg/day (N = 104), immediate-release paroxetine (paroxetine IR) up to 40 mg/day (N = 106), or placebo (N = 109). Patients met DSM-IV criteria for major depressive disorder and had a total score of 18 or more on the 17-item Hamilton Rating Scale for Depression (HAM-D). The primary efficacy measure was change from baseline to endpoint in HAM-D total score.

**RESULTS:** The primary efficacy analysis showed an adjusted difference between change from baseline in HAM-D score for paroxetine CR and placebo of -2.6 (95% confidence interval [CI] = -4.47 to -0.73,  $p = .007$ ) at the week 12 last-observation-carried-forward (LOCF) endpoint. The adjusted difference between paroxetine IR and placebo was -2.8 (95% CI = -4.65 to -0.99,  $p = .003$ ) at week 12. Paroxetine CR and IR were more effective than placebo, with mean +/- SD endpoint HAM-D total scores of 10.0 +/- 7.41 and 10.0 +/- 7.10, respectively, for the active treatments compared with 12.6 +/- 7.34 for placebo. Response, defined as a score of 1 or 2 on the Clinical Global Impressions-global improvement scale, was achieved by 72% of paroxetine CR patients (LOCF;  $p < .002$  vs. placebo), 65% of paroxetine IR patients ( $p = .06$  vs. placebo), and 52% of placebo patients. Remission, defined as a HAM-D total score  $\leq 7$ , was achieved by 43% of paroxetine CR patients (LOCF;  $p = .009$  vs. placebo), 44% of paroxetine IR patients ( $p = .01$  vs. placebo), and 26% of placebo patients. In a post hoc analysis, mean HAM-D improvement for paroxetine CR and paroxetine IR was greater than for placebo in both chronically depressed patients (duration  $> 2$  years) and those with short-term ( $\leq 2$  years) depression. Dropout rates due to adverse events were 12.5% for paroxetine CR, 16.0% for paroxetine IR, and 8.3% for placebo.

**CONCLUSION:** Paroxetine CR and paroxetine IR are effective and well-tolerated treatments for major depressive disorder in elderly patients, including those with chronic depression.