

# Express Scripts

## RESEARCH STUDY FINDINGS

### Prevalence of Antidepressant Use in Children: 2003 - 2004

In a study published this year, Express Scripts' researchers reported an increase in the prevalence of antidepressants from 1.6 per 100 to 2.4 per 100 continuously eligible child beneficiaries from 1998 to 2002 or an adjusted annual increase of 9.2%.<sup>1</sup> The study examined antidepressant use among approximately two million commercially-insured, pediatric beneficiaries 18 years and younger from 1998 to 2002. The fastest growing segment of users were found to be preschoolers aged 0-5 years, with use among girls doubling and use among boys growing by 64%.

Throughout the five-year period of the study, selective serotonin reuptake inhibitors (SSRI's) were the most commonly dispensed antidepressants, while tetracyclics were the least. SSRI's include paroxetine (also known as Paxil(R)), Prozac(R) and Zoloft(R). Use of paroxetine increased 113% and 91% in females and males, respectively, over the study period.

Since completing this study, several developments around antidepressant use in children have surfaced. In October 2003, the FDA issued a Public Health Advisory to healthcare professionals in response to its preliminary review of several studies that showed there may be a trend toward increased suicidal thinking in children taking certain antidepressants. In February 2004, an advisory committee urged the U.S. Food and Drug Administration (FDA) to strengthen its warnings to doctors and consumers about this potential risk. In March 2004, the FDA requested that the manufacturers of ten antidepressants update their labels to reflect more specific warnings and monitoring parameters related to the possible link that the medications may have to suicidal thinking. The drugs of concern include: bupropion (Wellbutrin® - GlaxoSmithKline (GSK), generics), citalopram (Celexa® - Forest), escitalopram (Lexapro® - Forest), fluoxetine (Prozac® - Eli Lilly, generics), fluvoxamine (Luvox® - Solvay, generics), mirtazapine (Remeron® - Organon, generics), nefazodone (Serzone® - Bristol-Myers Squibb, generics), paroxetine (Paxil® - GSK, generics), sertraline (Zoloft® - Pfizer), and venlafaxine (Effexor® - Wyeth). The FDA suggested that the warning statements should include careful monitoring of both adult and pediatric patients for possible worsening of depression or suicidal behavior, especially at the beginning of therapy and with dosing changes. The FDA is also advising that physicians evaluate whether the medication be continued in patients who develop severe symptoms such as panic attacks, hostility, impulsivity, and mania.

The Public Health Advisory can be found at:

[www.fda.gov/cder/drug/antidepressants/AntidepressantPHA.htm](http://www.fda.gov/cder/drug/antidepressants/AntidepressantPHA.htm)

<sup>1</sup> Delate T, Gelenberg AJ, Simmons VA, Motheral BR. Trends in the use of antidepressants in a national sample of commercially insured pediatric patients. 1998 to 2002. *Psychiatric Services* 2004;55:387-391.

As a result of these recent developments and in an effort to continue to monitor the prescribing of antidepressants in children, Express Scripts evaluated antidepressant prescription claims data for 2003 and the first half of 2004 for a sample of over 5 million commercially insured children 0 to 19 years of age. Children selected for inclusion in the study were enrolled in commercial plans (i.e., not Medicaid) with a subsidized benefit (e.g., not 100% copay plans) and were enrolled in plans that were clients of Express Scripts in 2003 and 2004. Antidepressant therapy classes evaluated included SSRIs (e.g., citalopram, fluoxetine, escitalopram, paroxetine, and sertraline), tricyclics (e.g., amitriptyline, desipramine, nortriptyline), modified cyclics (e.g., nefazodone and trazodone), tetracyclics (mirtazapine), and miscellaneous antidepressants (e.g., maprotiline, bupropion, and venlafaxine). Prevalence of use was defined as the number of children 0 to 19 years of age with at least one prescription claim for an antidepressant in each quarter, divided by the total number of children 0 to 19 years of age enrolled in that quarter.

## Results

Our results indicate that the prevalence of antidepressant use in children continued to rise through the first half of 2004. The overall rate of antidepressant use in children grew from 1.47% in the first quarter of 2003 to 1.61% in first quarter 2004, a 9.4% increase in the prevalence of use. This increase in the prevalence of use moderated through the second quarter of 2004, slowing from 9.4% in the first quarter to just under 3% in the second quarter. The growth in the rate of use was primarily driven by teenagers age 10 to 14 and 15 to 19 years, whereas children 9 years of age and younger saw much lower and even negative rates of growth from the first half of 2003 compared to the first half of 2004. Consistent with our previous research<sup>1</sup>, the highest prevalence of antidepressant use was found in children 15 to 19 years of age with prevalence rates above 3% in 2003 and approaching 4% in the first quarter of 2004. Contrary to our previous work, the change in absolute prevalence decreased in the first half of 2004 for children 0 to 4 years of age and decreased in the second quarter for children 5 to 9 years of age.

Table: Quarterly prevalence of and percent change in antidepressant use per 100 child beneficiaries 0 to 19 years of age: 2003-2004

Prevalence per 100 children							Absolute change quarter to quarter in prevalence per 100 child beneficiaries	
Age Group	Q1 2003	Q2 2003	Q3 2003	Q4 2003	Q1 2004	Q2 2004	Q103-Q104	Q203-Q204
0-4 yrs	0.049%	0.050%	0.043%	0.040%	0.036%	0.036%	-0.013	-0.014
5-9 yrs	0.555%	0.549%	0.527%	0.560%	0.579%	0.536%	0.024	-0.013
10-14 yrs	1.651%	1.687%	1.602%	1.738%	1.818%	1.741%	0.167	0.054
15-19 yrs	3.244%	3.309%	3.176%	3.431%	3.577%	3.430%	0.334	0.121
<b>0-19 yrs</b>	<b>1.473%</b>	<b>1.499%</b>	<b>1.433%</b>	<b>1.547%</b>	<b>1.612%</b>	<b>1.541%</b>	<b>0.139</b>	<b>0.041</b>

## Conclusions

The growth in the prevalence of antidepressant use in children continued to increase into 2004, however rates of use appear to moderate for teens and decrease for children under the age of 9 in the second quarter of 2004. It is unclear whether the decrease in use among children 9 and under was due to the FDA Advisory on increased risk of suicide in children, particularly since the studies documenting this increased risk were in children no younger than 7 years (youngest age range was from 7 to 9 years).

On September 21, the New York Times reported results of a study that found that the number of children on antidepressants decreased 18% in the first quarter of 2004. While our findings did not show such a dramatic decrease in use overall, our findings do suggest a significant decrease in use among younger children (ages 9 and younger) and an overall moderation in the growth during the second quarter of 2004.

Currently, fluoxetine is the only drug approved for use in the treatment of pediatric depression. The FDA is continuing to review clinical studies involving antidepressant use in children in order to determine if there is clear evidence that some or all of the agents increase the risk of suicidal thinking and behavior. There have been no reports of completed suicides in any of the trials being reviewed. The FDA plans to report the results of this review very soon.

While stronger warning labels on antidepressants may draw increased attention to the issue of suicide risk in depressed children, antidepressant prescribing for this population will likely continue, albeit with more caution. Antidepressants are used to treat other mental health conditions in children, such as obsessive-compulsive disorder, anxiety disorders, and bulimia, and to this point studies have not shown an increased risk of suicide in these patient populations. In addition, effective treatment alternatives for depression remain limited.

Through our concurrent drug use review (cDUR) system, Express Scripts sends point of service messages to pharmacists alerting them to the potential risks of antidepressant use in children. Should there be additional FDA advisories or directives, we will make corresponding changes to this system.