

North Dakota Medicaid
Drug Utilization Review Board
Drug Class Review

Attention Deficit Hyperactivity Disorder (ADHD) Agents

Prepared by Health Information Designs, Inc.

**North Dakota Department of Social Services
Pharmacotherapy Review
Medications for ADHD
August 20, 2007**

I. Overview

Most medications for ADHD are CNS stimulants, which are thought to work by blocking reuptake of norepinephrine and dopamine in the presynaptic neurons and increasing release of these neurotransmitters into the extraneural space. There is one non-stimulant medication for ADHD, atomoxetine (Strattera®), which is thought to work by a different mechanism. Atomoxetine is classified as a norepinephrine reuptake inhibitor and works by selectively inhibiting presynaptic norepinephrine transporters.¹

ADHD is a pervasive childhood problem, affecting approximately 3 to 5% of school age children. This amounts to about 2 million children. To put that in perspective, in a class of 25 to 30 children, it is likely that at least one child will be affected by ADHD.^{2,3} Children with ADHD are usually diagnosed between the ages of 6 to 12, as it is hard to diagnose much earlier than that. A diagnosis of ADHD is subjective in nature, with the provider looking for symptoms of inattention, hyperactivity, and impulsivity; symptoms that are frequent and severe enough to interfere with the child's and often, the family's ability to lead a normal life. These children, left undiagnosed or untreated, are at higher risk of self-injury, depression, low self-esteem, and a host of other societal disorders.³⁻⁵

Pharmacotherapy, along with behavior therapy and counseling, can certainly help those patients diagnosed with ADHD lead a normal and productive life.³ For many years, CNS stimulants have been considered first-line therapy for the treatment of ADHD. With the approval of atomoxetine in late 2002, patients now have another treatment option.⁶ Table 1 lists the medications included in this review. This review encompasses all dosage forms and strengths.

Table 1. ADHD Medications in this Review

Generic Name	Brand Name
Amphetamine mixture	Adderall®, Adderall XR
Atomoxetine	Strattera®
Dexmethylphenidate	Focalin®, Focalin XR®
Dextroamphetamine	Dexedrine®, Dexedrine spansule®, Dextrostat®
Lisdexamfetamine	Vyvanse®
Methylphenidate	Ritalin®, Ritalin SR®, Ritalin LA®, Concerta®, Metadate ER®, Metadate CD®, Methylin ER®, Methylin®, Daytrana® Patch

II. Current Treatment Guidelines

In October 2004, the American Academy of Child and Adolescent Psychiatry (AACAP) issued a new, multi-tiered treatment plan:⁷

- 1) Identify target behavior symptom(s) and collect previous treatment data.
- 2) Develop a treatment plan that involves drug and/or behavioral therapy and involves parents, teachers and caregivers. It is also important to recognize that ADHD is a chronic condition. Up to 80% of those diagnosed will continue taking medication through adolescence and 65% will continue through adulthood.²
- 3) Define appropriate target outcomes, so that medication effectiveness can be clearly and systemically evaluated. It is important to define clear goals – control of symptoms at school, at home, or both – so that it can be determined whether or not a child needs long-acting, short-acting, or a combination of the two types of medication.⁷
- 4) Medication selection:
 - a. CNS stimulants are still considered to be first-line therapy as 70 to 80% of children respond favorably to this class. Of note, response to one stimulant medication does not predict response to another.⁸
 - b. Atomoxetine is also considered to be first-line therapy in patients where a stimulant is contraindicated (patients with tics, psychosis, or certain cardiovascular conditions), where parent or physician does not want a stimulant medication used, or in cases where the risk of drug diversion or abuse is high.⁷
 - c. Tricyclic antidepressants, bupropion, and clonidine are used, but are considered second line therapy, to be used only after 2 or more stimulants and atomoxetine have been tried and failed.⁸

III. Comparative Indications for ADHD Medications

A diagnosis of ADHD (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition [DSM-IV]) implies the presence of hyperactive-impulsive or inattentive symptoms that cause impairment and are present before 7 years of age. There are three subtypes of ADHD: inattentive, hyperactive-impulsive, and combined.⁴ All medications included in this review are indicated for ADHD. Although it is recognized that ADHD is a chronic condition, few of these medications have been studied for long-term use.⁹⁻¹⁷

IV. Pharmacokinetic Parameters of ADHD Medications

The kinetic parameters of these medications vary due to the need for short, intermediate, and long-acting therapy. All of the medications for ADHD, with the exception of atomoxetine, are excreted in the urine and are unaffected by hepatic or renal impairment. Atomoxetine is metabolized by CYP2D6 system and dosing adjustments must be made in moderate to severe hepatic impairment. Tables 2-4 summarize various pharmacokinetic parameters for these medications.

Table 2. Pharmacokinetic Parameters of Short-Acting (3-5 hours) ADHD Medications^{1, 9-17}

	Time to peak	Metabolizing mechanism	Effects of hepatic/renal impairment
Adderall	3 hours	-	No effect
Dexedrine [†]	3 hours	-	No effect
Focalin	1 to 1½ hours	90% excreted in urine	No effect
Ritalin [*]	1.9 hours	86% excreted in urine	No effect

[†]Dextrostat thought to have similar kinetic parameters.

^{*}Methylin thought to have similar kinetic parameters

Table 3. Pharmacokinetic Parameters of Intermediate-Acting (6-8hours) ADHD Medications^{1,9-17}

	Time to peak	Metabolizing mechanism	Effects of hepatic/renal impairment
Dexedrine spansules	8 hours	-	No effect
Ritalin SR [†]	4.7 hours	67% excreted in urine	No effect
Metadate CD	1 st peak 1.5 hours 2 nd peak 4.5 hours	-	-
Ritalin LA	1 st peak 1 to 3 hours 2 nd peak 4 hours after dose intake	78 to 97% excreted in urine	No studies available; expected to have little effect
Focalin XR	1 st peak 1½ hours 2 nd peak 4 hours after dose intake	~ 90% excreted in urine	Expected to have little effect

[†]Methylin ER and Metadate ER expected to have similar kinetic parameters.

Table 4. Pharmacokinetic Parameters of Long-Acting (10-24 hours) ADHD Medications^{1,9-17}

	Time to peak	Metabolizing mechanism	Effects of hepatic/renal impairment
Adderall XR [†]	7 hours	1 to 75% excreted in urine; dependent upon urinary pH. Minor amounts excreted through CYP2D6 system	Can be affected; dependent on urinary pH; alkaline urine may increase hepatic elimination thereby increasing need for dose adjustments.
Concerta	1 st peak 1 hour; ascending concentrations over next 5 to 9 hours	90% excreted in urine	No effect
Strattera [†]	1 to 2 hours	98% protein bound; eliminated through the CYP2D6 system	Dosage adjustments needed in moderate to severe hepatic impairment.*

[†]Vyvanse expected to have similar kinetic parameters.

[†]Takes 4 to 6 weeks to reach optimal therapeutic efficacy.

*Dosing guidelines for hepatic impairment included in prescribing information.

V. ADHD Medication Drug Interactions

Clinically important drug interactions exist for the ADHD medications with certain, important differences among the classes. Each of the medications in this class should be used cautiously with antihypertensives (as stimulants, and atomoxetine, may antagonize the effects of antihypertensive medications), tricyclic antidepressants, and MAO inhibitors. (can result in hypertensive crisis).^{1,9-17}

Amphetamines

- GI acidifying agents (ascorbic acid, guanethidine, fruit juice) decrease absorption of amphetamines and urinary acidifiers (aluminum chloride) increase excretion of amphetamines.
- GI alkalinizers (sodium bicarb) increase absorption of amphetamines and urinary alkalinizers (acetazolamide) decrease excretion of amphetamines.
- Chlorpromazine/haloperidol block dopamine/norepinephrine receptors decreasing effects of amphetamines.
- Lithium carbonate inhibits stimulatory effects of amphetamines.

- Meperidine activity is potentiated by amphetamines.
- Co-administration of phenobarbital and phenytoin with amphetamines may lead to a synergistic anticonvulsant action.

Methylphenidate and Dexmethylphenidate

- May decrease metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, phenytoin, and primidone), and antidepressants (TCA's and SSRI's) resulting in the need for dosage adjustments.
- Serious adverse events have been noted with concomitant use of clonidine, although no causality has been established. This combination should be carefully monitored if use is deemed therapeutically necessary.

Atomoxetine

- Paroxetine, fluoxetine, and quinidine are all CYP2D6 inhibitors, dosing of atomoxetine may need to be adjusted when given with any of these medications.
- The effects of albuterol on heart rate and blood pressure may be potentiated by atomoxetine.

Most of the drug interactions listed above can be managed with dosing modifications and monitoring. When considering the population commonly treated for ADHD, mainly children and adolescents, treatment with any of the ADHD medications should not be precluded due to any harmful drug interactions.

VI. Comparative Adverse Effects of ADHD Medications

Because ADHD medications are commonly given to children, adverse effects are of major concern.

On February 21, 2007, the FDA directed all manufacturers of products approved for the treatment of ADHD to develop Patient Medication Guides to alert patients to possible cardiovascular risks and risks of adverse psychiatric symptoms associated with the medicines, and to advise them of precautions that can be taken.

An FDA review of reports of serious cardiovascular adverse events in patients taking usual doses of ADHD products revealed reports of sudden death in patients with underlying serious heart problems or defects, and reports of stroke and heart attack in adults with certain risk factors. FDA recommends that children, adolescents, or adults who are being considered for treatment with ADHD drug products work with their physician or other health care professional to develop a treatment plan that includes a careful health history and evaluation of current status, particularly for cardiovascular and psychiatric problems (including assessment for a family history of such problems).

In September 2005, the FDA issued an alert and the manufacturer of atomoxetine revised its labeling to include a black box warning about the risks of suicidal ideation. Patients started on atomoxetine should be monitored for suicidal thinking and behavior, clinical worsening of symptoms, and unusual changes in behavior. The risk of suicidal ideation in patients taking atomoxetine was 0.4% (5/1357 patients) versus none (0/851) in the placebo arm. There is no consensus yet as to the risk of suicidal ideation with the CNS stimulants. The FDA is conducting retrospective reviews of all medications for ADHD medications.^{15,18} Additionally, there have been postmarketing reports indicating that atomoxetine can cause severe liver damage in rare instances. In clinical trials with over 6,000 patients and postmarketing use in over 2 million patients, there have been 2 reported cases of serious liver injury. Because of this information, atomoxetine should be discontinued and liver function testing should be performed at the first sign of liver injury (jaundice, dark urine, or unexplained flu-like symptoms).^{15,19}

Rare reports of NMS (neuroleptic malignant syndrome) have occurred with dexamethylphenidate and methylphenidate. In most cases, patients were receiving therapies associated with NMS. It is not known whether this is a drug/drug interaction, a reaction to one drug alone, or due to some other cause.¹²⁻¹⁴

In regard to other adverse reactions, many similarities exist between the drugs used to treat ADHD. Tachycardia, increased blood pressure, anorexia, weight loss, and sleep pattern disturbances are of major concern, especially in this population of patients. Dry mouth, restlessness, and urticaria are also commonly seen with this class of medications. And with the exception of atomoxetine, all medications carry the risk of exacerbating tics and Tourette's syndrome.¹ One consideration to note, it has been clearly demonstrated that patients who do not respond well to one stimulant medication may respond to another.⁸ Table 5 lists the adverse reactions reported with the most commonly prescribed medications for ADHD. Incidences of adverse effects are listed as percentages with the placebo incidence listed in parentheses.

Table 5. Adverse Reactions (%) Reported with Selected ADHD Medications

	Abdominal pain	Loss of appetite	Insomnia	Weight loss
Adderall XR				
Children	14% (10)	22% (2)	17% (2)	4% (0)
Adolescents	11% (2)	36% (2)	12% (4)	9% (0)
Adults	8% (3)	33% (3)	27% (13)	11% (0)
Concerta				
Children	7% (1)	4% (0)	4% (1)	N/L
Adolescents	N/L	2% (0)	5% (0)	N/L
Daytrana	N/L	26%	13%	9%
Focalin	15% (6)	6% (1)	N/L	N/L
Focalin XR	[general GI disorders]		[general NS disorders]	
Children/Adolescents	38% (19)	30% (9)	34% (11)	N/L
Adults	28-44% (19)	N/L	37-50% (28)	N/L
Metadate CD	7% (4)	9% (4)	5% (2)	N/L
Strattera				
Children	20% (16)	14% (6)	N/L	2% (0)
Adults	12% (5)	10% (6)	N/L	N/L
Ritalin LA	N/L	3% (0)	.% (0)	N/L
Vyvanse	12%	N/L	2%	9%

N/L = percentage results not listed in prescribing information.

One final consideration – all CNS stimulants have reported suppression of growth (weight gain and/or height) with long-term use. Although it appears that this a temporary delay and that the patients will normalize in late adolescence, children should be monitored for height and weight changes while taking a CNS stimulant.^{20,21}

VII. Dosing and Administration of ADHD Medications

The newer, longer-acting ADHD medications are designed so that children can take them once-a-day. There are still some children who will require a noon or late afternoon dose. Newer drugs offer a distinct advantage over the older, more traditional medications in that the majority of patients can do with once daily dosing. Table 6 details dosing and administration guidelines for the drugs in this class.

Table 6. ADHD Medication Dosing & Administration^{1,7}

Brand Name	Dosage Form	Typical Starting Dose	FDA max/day	Off-label max/day	Comments	
Amphetamine Preparations						
Short-acting						
<i>Adderall</i> *	5, 7.5, 10, 12.5, 15, 20, 30 mg tabs	3-5yr: 2.5 mg qd ≥6yr: 5 mg qd-bid	40 mg	>50 kg: 60 mg	*All of these medications are classified as C-II narcotics. *Adderall XR may be opened and sprinkled on soft food.	
<i>Dexedrine</i> *	5 mg tab					
<i>Dextrostat</i> *	5, 10 mg tabs					
Long-acting						
<i>Dexedrine Spansule</i>	5, 10, 15 mg caps	≥6yr: 5 mg qd-bid	40 mg	>50 kg: 60mg		
<i>Adderall XR</i>	5, 10, 15, 20, 25, 30 mg caps	≥6yr: 10 mg qd	30 mg	>50 kg: 60mg		
<i>Vyvanse</i>	30, 50, 70 mg caps	30 mg qd	70 mg	Not yet known		
Methylphenidate Preparations						
Short-Acting (3-4 hours)						
<i>Focalin</i>	2.5, 5, 10 mg tabs	2.5 mg bid	20 mg	50 mg	*Metadate CD, and Ritalin LA caps may be opened and sprinkled on soft food. *All of these medications are C-II narcotics.	
<i>Methylin</i> *	5, 10, 20 mg tabs	5 mg bid	60 mg	>50 kg: 100 mg		
<i>Ritalin</i> *						
Intermediate-Acting (6-8 hours)						
<i>Metadate ER</i>	10, 20 mg tabs	10 mg q am	60 mg	>50 kg: 100 mg		
<i>Methylin ER</i>	10, 20 mg tabs					
<i>Ritalin SR</i> *	20 mg tab					
<i>Metadate CD</i>	10, 20, 30, 40, 50, 60 mg caps	20 mg q am	60mg	>50 kg: 100 mg		
<i>Ritalin LA</i>	10, 20, 30, 40 mg caps					
Long-Acting (12+ hours)						
<i>Focalin XR</i>	5, 10, 15, 20 mg tabs	5 mg q am	30 mg	50 mg	*Concerta tab should be swallowed whole – nonabsorbable tab shell may be seen in stool. *All of these medications are C-II narcotics. *Daytrana should be applied to hip area 2 hours before effect is needed and should be removed 9 hours after application.	
<i>Concerta</i>	18, 27, 36, 54 mg tabs	18 mg q am	72 mg	108 mg		
<i>Daytrana</i>	10, 15, 20, 30 mg patches	Begin with 10 mg patch qd, then titrate up weekly by patch strength	30 mg	Not yet known		

Atomoxetine (24 hours)					
Strattera	10, 18, 25, 40, 60, 80, 100 mg caps	Children and adolescents <70 kg: 0.5mg/kg/day for 4 days then 1.2mg/kd/day	Lesser of 1.4mg/kg or 100 mg	Lesser of 1.8mg/kg or 100 mg	*Not a scheduled medication. *Do <u>not</u> open capsule and sprinkle. *May give qd or divided bid.

VIII. Effectiveness

Table 6. Comparative Clinical Trials

Study	Sample	Duration	Results
MTA ^{22,23}	n = 579 ages 7-9.9 years	14 months	Compared routine community care, medication management, behavioral therapy, and combination therapy. Resulted in: *children showed most improvement with medication management and combination therapy.
Atomoxetine and MPH ²²	n = 228	10 weeks	Compared atomoxetine to methylphenidate. Response assessed with ADHD-IV rating scale. Resulted in: *children in both groups showed marked improvement. *no statistically significant difference in primary outcome. *safety and tolerance profiles are similar with both drugs.
QD Concerta vs TID MPH ²³	n = 68 ages 6-12 years patients stable on MPH	7 days	Compared once daily concerta to three times a day methylphenidate. Response assessed by DRC. Resulted in: *2 parent rating scores showed that parents preferred daily dosing. *no statistically significant differences in side effects. *both drugs are equally efficacious.
Once Daily MPH ²⁶	n = 407 ages 6-13 years OROSMPH (18-54mg)	24 months	*71% (229/407) finished the study. *MPH had minimal impact on sleep quality and tics. *No clinically significant effects on blood pressure,

			<p>pulse, or height.</p> <p>*26% of patients had to increase their mean daily dose.</p> <p>*7.6% (31/407) discontinued the study due to adverse effects.</p>
MPH vs placebo ²⁷	<p>n = 72</p> <p>ages 5-14 years</p> <p>drug-free</p>	8 weeks	<p>Study resulted in:</p> <p>*49% (35/72) were MPH responders.</p> <p>*18% (13/72) discontinued due to adverse reactions.</p> <p>*MPH demonstrated to be superior to placebo in primary outcomes.</p>
ER-MPH vs OROS MPH ²⁸	<p>n = 53</p> <p>ages 6-12 years</p> <p>stabilized on MPH 40mg/day</p>	6 weeks	<p>ER-MPH 20 and 40mg compared to OROS MPH 18 and 36mg. Resulted in:</p> <p>*efficacy of ER-MPH 20mg is similar to OROS MPH 18 & 36mg during first 8 hours post dose.</p> <p>*statistically greater benefit with ER-MPH 40mg than with OROS MPH 36mg.</p> <p>*both dosage forms were well tolerated.</p>
CV effects in MAS ²⁹	<p>short-term n = 580</p> <p>long-term n = 568</p> <p>ages 6-12 years</p> <p>stabilized on mixed amphetamine salts extended release 10-30mg/day</p>	<p>short-term – 4 weeks</p> <p>long-term – 2 years</p>	<p>Study resulted in:</p> <p>*changes in bp, pulse, QT interval not statistically significant in short-term treatment.</p> <p>*mean increase in bp and pulse after 2 years (systolic = 3.5mmHg; diastolic = 2.6mmHg; pulse = 3.4bpm) clinically insignificant.</p>
Atomoxetine vs placebo ³⁰	<p>n = 153</p> <p>ages 8-12 years</p>	7 weeks	<p>Atomoxetine compared to placebo. Resulted in:</p> <p>*ADHDRS-IV Teacher: Inv subscales significantly lower for children treated with atomoxetine.</p> <p>*5.9% of children on atomoxetine discontinued study due to side effects vs 0% of children on placebo.</p>
Long-term Adderall XR use ³¹	<p>n = 568</p> <p>ages 6-12 years</p>	24 months	<p>Resulted in:</p> <p>*significant increases in CGIS-P scores were maintained over study period.</p> <p>*drug was well tolerated – adverse events seem to increase as dose increases.</p>

Evaluation of d-methylphenidate ³²	n = 22 ages 6-18 years	8 weeks	Resulted in: *85.7% (18/21) showed at least a 30% improvement on CTPR scales. *86.4% (19/22) showed at least a 30% improvement on the CPR scale.
Drug Diversion ³³	n = 1536 grades 6-11 81% of those surveyed planned to attend college	Survey	Looking at use, misuse, and diversion of prescribed stimulants. *illicit use reported by 4.5% of sample group. *23.3% reported being approached to sell, give, or trade their medication.

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts & Comparisons. St. Louis, MO. 2005.
2. Dulcan M, Benson RS. Summary of the Practice Parameters for the Assessment and Treatment of Children, Adolescents, and Adults with ADHD. Adopted March 1997. Accessed at www.aacap.org.
3. Children Who Can't Pay Attention: Facts For Families. AACAP. July 2004.
4. Committee on Quality Improvement, Subcommittee on ADHD (2000), Clinical Practice Guideline: Diagnosis and Evaluation of the Child with ADHD. *Pediatrics* 105: 1158-1170.
5. ICSI Health Care Guideline: Diagnosis and Management of ADHD in Primary Care for School Age Children and Adolescents. 6th Ed. January 2005. Accessed at www.icsi.org.
6. LoBuono C. Nonstimulant Now First-Line Option for ADHD. *Drug Topics*. June 2004;148:36.
7. American Academy of Child and Adolescent Psychiatry (2002), Practice Parameters for the Use of Stimulant Medications in the Treatment of Children, Adolescents, and Adults. *J Am Acad Child Adolesc Psychiatry* 41:26S-49S.
8. American Academy of Pediatrics (AAP): Subcommittee on ADHD and Committee on Quality Improvement. Clinical Practice Guideline: Treatment of School-Aged Children with ADHD. *Pediatrics* Vol 108 No. 4 October 2001, pp. 1033-44.
9. Adderall XR[®] [prescribing information]. Wayne, PA: Shire US Inc; 2005.
10. Concerta[®] [prescribing information]. Fort Washington, PA: ALZA Corp; October 2004.
11. Dexedrine[®] [prescribing information]. Research Triangle Park, NC: Glaxo Smith Kline; October 2005.
12. Focalin[®] [prescribing information]. East Hanover, NJ: Novartis; November 2001.
13. Focalin XR[®] [prescribing information]. East Hanover, NJ: Novartis; May 2005.
14. Ritalin LA[®] [prescribing information]. East Hanover, NJ: Novartis; April 2004.
15. Strattera[®] [prescribing information]. Indianapolis, IN: Eli Lilly and Company; November 2005.
16. Vyvanse[®] [prescribing information]. Wayne, PA: Shire US Inc.; February 2007.
17. Daytrana[®] [prescribing information]. Ireland: Shire Pharmaceuticals Ireland Limited; 2007.
18. FDA Alert. P05-65. Issued September 29, 2005.
19. FDA Alert. T04-60. Issued December 17, 2004.
20. Spencer T, Biedeman J, Wilens T. Growth Deficits in Children with ADHD. *Pediatrics* Vol 102 No. 2 Supplement August 1998, pp 501-506.
21. Zachor DA, Roberts AW, Bart HJ, et al. Effects of long-term psychostimulant medication on growth of children with ADHD. *Res Dev Disabil* 2005 Jun 11.
22. Jensen PS, Hinshaw SP, Swanson JM, et al. Findings from the NIMH Multimodal Treatment Study of ADHD (MTA): Implications and Applications for Primary Care Providers. *Journal of Developmental and Behavioral Pediatrics*. 22(1):60-73, February 2001.
23. MTA Cooperative Group. A 14-Month Randomized Clinical Trial of Treatment Strategies for ADHD. *Arch Gen Psychiatry*. 1999;56:1073-1086.
24. Kratochival CJ, Heiligenstein JH, Dittman R, et al. Atomoxetine and Methylphenidate Treatment in Children with ADHD: A Prospective, Randomized, Open-Label Trial. *Journal of the American Academy of Child and Adolescent Psychiatry*. 41(7):776-784, July 2002.
25. Pelham WE, Gnagy EM, Burrows-Maclean L, et al. Once-a-Day Concerta Versus Three-Times-Daily Methylphenidate in Laboratory and Natural Settings. *Pediatrics*. Vol 107 No. 6 June 2001, p105.
26. Wilens T, McBurnett K, Stein M, et al. ADHD Treatment With Once-Daily OROS Methylphenidate: Final Results From a Long-Term Open-Label Study. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2005 Oct;44(10):1015-23.
27. Research Units on Pediatric Psychopharmacology (RUPP) Autism Network. Randomized, Controlled, Crossover Trial of Methylphenidate in Pervasive Developmental Disorders with Hyperactivity.
28. Silva R, Muniz R, Pestreich LK, et al. Efficacy of two long-acting methylphenidate formulations in children with ADHD in a laboratory classroom setting. *J Child Adolesc Psychopharmacol*. 2005 Sept;15(4):637-54.

29. Findling RL, Biederman J, Wilens TE, et al. Short- and Long-Term CV Effects of Mixed Amphetamine Salts Extended Release in Children. *J Pediatrics*. 2005 Sep, 147(3):286-7.
30. Weiss M, Tannock R, Kratochvik C, et al. A Randomized, Placebo Controlled Study of Once-Daily Atomoxetine in the School Setting in Children with ADHD. *J Am Acad Child Adolesc Psychiatry*. 2005 Jul; 44(7):647-55.
31. Mcgough JJ, Biederman J, Wigal SB, et al. Long-Term Tolerability and Effectiveness of Once-Daily Mixed Amphetamine Salts (Adderall XR) in Children with ADHD. *J Am Acad Child Adolesc Psychiatry*. 2005 Jun; 44(6):530-38.
32. Silva R, Tilker HA, Cecil JT, et al. Open label study of dexamethylphenidate hydrochloride in children and adolescents with ADHD. *J Child Adolesc Psychopharmacol*. 2004 Winter; 14(4):555-63.
33. McCabe SE, Teter CJ, Boyd CJ. The use, misuse, and diversion of prescription stimulants among middle high and high school students. *Subst Use Misuse*. 2004 Jun; 39(7):1095-116.

North Dakota Medicaid Statistics

The table below includes actual North Dakota Medicaid utilization of the products in this review category from 4/1/2006 through 3/31/2007.

Label Name	Total Reimb Amt	Rx Num
ADDERALL 10 MG TABLET	\$1,401.71	9
ADDERALL 20 MG TABLET	\$2,745.38	20
ADDERALL 30 MG TABLET	\$7,095.58	36
ADDERALL XR 10 MG CAPSULE SA	\$68,554.19	682
ADDERALL XR 15 MG CAPSULE SA	\$62,594.05	664
ADDERALL XR 20 MG CAPSULE SA	\$193,597.34	1545
ADDERALL XR 25 MG CAPSULE SA	\$46,370.33	438
ADDERALL XR 30 MG CAPSULE SA	\$136,683.43	1267
ADDERALL XR 5 MG CAPSULE SA	\$18,435.66	209
AMPHETAMINE SALTS 5MG TAB	\$11,120.18	257
AMPHETAMINE SALTS 7.5MG	\$395.64	5
AMPHETAMINE SALTS 10MG TAB	\$30,128.21	619
AMPHETAMINE SALTS 15MG TAB	\$2,098.16	38
AMPHETAMINE SALTS 20MG TAB	\$19,018.78	375
AMPHETAMINE SALTS 30MG TAB	\$12,759.41	211
CONCERTA 18 MG TABLET SA	\$68,309.53	770
CONCERTA 27 MG TABLET SA	\$79,101.17	909
CONCERTA 36 MG TABLET SA	\$278,537.14	2437
CONCERTA 54 MG TABLET SA	\$239,965.73	2401
D-AMPHETAMINE 10 MG CAP SA	\$14,448.15	321
D-AMPHETAMINE 15 MG CAP SA	\$14,891.09	300
D-AMPHETAMINE 5 MG CAP SA	\$653.27	26
DAYTRANA 10 MG/9 HR PATCH	\$9,512.54	100
DAYTRANA 15 MG/9 HR PATCH	\$8,656.88	82
DAYTRANA 20 MG/9 HOUR PATCH	\$10,129.80	124
DAYTRANA 30 MG/9 HOUR PATCH	\$8,810.84	78

Label Name	Total Reimb Amt	Rx Num
DEXEDRINE 5 MG TABLET	\$250.50	4
DEXEDRINE SPANSULE 10 MG	\$565.87	11
DEXEDRINE SPANSULE 15 MG	\$2,101.14	23
DEXTROAMPHETAMINE 10 MG TAB	\$5,335.76	176
DEXTROAMPHETAMINE 5 MG TAB	\$4,329.09	254
DEXTROSTAT 10 MG TABLET	\$885.66	10
FOCALIN 10 MG TABLET	\$5,846.28	118
FOCALIN 2.5 MG TABLET	\$1,287.63	58
FOCALIN 5 MG TABLET	\$6,015.55	154
FOCALIN XR 10 MG CAPSULE	\$32,798.56	360
FOCALIN XR 15 MG CAPSULE	\$5,009.95	46
FOCALIN XR 20 MG CAPSULE	\$34,004.14	372
FOCALIN XR 5 MG CAPSULE	\$20,022.37	228
METADATE CD 10 MG CAPSULE	\$15,901.64	231
METADATE CD 20 MG CAPSULE	\$72,141.85	738
METADATE CD 30 MG CAPSULE	\$32,209.54	347
METADATE CD 40 MG CAPSULE	\$7,798.94	73
METADATE CD 50 MG CAPSULE	\$1,296.36	9
METADATE CD 60 MG CAPSULE	\$585.54	4
METADATE ER 20 MG TABLET SA	\$184.60	5
METHYLIN 10 MG TABLET	\$20,594.75	964
METHYLIN 10 MG/5 ML SOLUTION	\$1,039.83	21
METHYLIN 20 MG TABLET	\$15,070.19	472
METHYLIN 5 MG TABLET	\$9,086.20	522
METHYLIN ER 10 MG TABLET SA	\$2,466.47	90
METHYLIN ER 20 MG TABLET SA	\$4,320.04	161
METHYLPHENIDATE 10 MG TABLET	\$6,233.79	293
METHYLPHENIDATE 20 MG TABLET	\$9,855.45	285

Label Name	Total Reimb Amt	Rx Num
METHYLPHENIDATE 5 MG TABLET	\$2,003.15	118
METHYLPHENIDATE ER 20 MG TAB	\$3,007.31	103
RITALIN 10 MG TABLET	\$224.37	5
RITALIN 20 MG TABLET	\$2,969.70	23
RITALIN 5 MG TABLET	\$62.14	3
RITALIN LA 10 MG CAPSULE	\$13,102.54	141
RITALIN LA 20 MG CAPSULE	\$31,629.59	407
RITALIN LA 30 MG CAPSULE	\$35,984.80	465
RITALIN LA 40 MG CAPSULE	\$38,718.25	443
RITALIN-SR 20 MG TABLET SA	\$296.40	5
STRATTERA 10 MG CAPSULE	\$21,460.00	187
STRATTERA 100 MG CAPSULE	\$857.88	6
STRATTERA 18 MG CAPSULE	\$26,016.85	245
STRATTERA 25 MG CAPSULE	\$69,640.76	635
STRATTERA 40 MG CAPSULE	\$150,878.98	1145
STRATTERA 60 MG CAPSULE	\$57,299.92	556
STRATTERA 80 MG CAPSULE	\$11,026.10	79
TOTALS	\$2,128,430.62	24518

Utilization by Drug

Label Name	Total Reimb Amt	Rx Num
ADDERALL 10 MG TABLET	\$1,401.71	9
ADDERALL 20 MG TABLET	\$2,745.38	20
ADDERALL 30 MG TABLET	\$7,095.58	36
Totals	\$11,242.67	65
Label Name	Total Reimb Amt	Rx Num
AMPHETAMINE SALTS 5MG TAB	\$11,120.18	257
AMPHETAMINE SALTS 7.5MG TAB	\$395.64	5
AMPHETAMINE SALTS 10MG TAB	\$30,128.21	619
AMPHETAMINE SALTS 15MG TAB	\$2,098.16	38
AMPHETAMINE SALTS 20MG TAB	\$19,018.78	375
AMPHETAMINE SALTS 30MG TAB	\$12,759.41	211
Totals	\$75,520.38	1505
Label Name	Total Reimb Amt	Rx Num
ADDERALL XR 10 MG CAPSULE SA	\$68,554.19	682
ADDERALL XR 15 MG CAPSULE SA	\$62,594.05	664
ADDERALL XR 20 MG CAPSULE SA	\$193,597.34	1545
ADDERALL XR 25 MG CAPSULE SA	\$46,370.33	438
ADDERALL XR 30 MG CAPSULE SA	\$136,683.43	1267
ADDERALL XR 5 MG CAPSULE SA	\$18,435.66	209
Totals	\$526,235.00	4805
Label Name	Total Reimb Amt	Rx Num
CONCERTA 18 MG TABLET SA	\$68,309.53	770
CONCERTA 27 MG TABLET SA	\$79,101.17	909

CONCERTA 36 MG TABLET SA	\$278,537.14	2437
CONCERTA 54 MG TABLET SA	\$239,965.73	2401
Totals	\$665,913.57	6517
Label Name	Total Reimb Amt	Rx Num
D-AMPHETAMINE 10 MG CAP SA	\$14,448.15	321
D-AMPHETAMINE 15 MG CAP SA	\$14,891.09	300
D-AMPHETAMINE 5 MG CAP SA	\$653.27	26
Totals	\$29,992.51	647
Label Name	Total Reimb Amt	Rx Num
DAYTRANA 10 MG/9 HR PATCH	\$9,512.54	100
DAYTRANA 15 MG/9 HR PATCH	\$8,656.88	82
DAYTRANA 20 MG/9 HOUR PATCH	\$10,129.80	124
DAYTRANA 30 MG/9 HOUR PATCH	\$8,810.84	78
Totals	\$37,110.06	384
Label Name	Total Reimb Amt	Rx Num
DEXEDRINE 5 MG TABLET	\$250.50	4
Label Name	Total Reimb Amt	Rx Num
DEXEDRINE SPANSULE 10 MG	\$565.87	11
DEXEDRINE SPANSULE 15 MG	\$2,101.14	23
Totals	\$2,667.01	34
Label Name	Total Reimb Amt	Rx Num
DEXTROAMPHETAMINE 10 MG TAB	\$5,335.76	176
DEXTROAMPHETAMINE 5 MG TAB	\$4,329.09	254
Totals	\$9,664.85	430
Label Name	Total Reimb Amt	Rx Num
DEXTROSTAT 10 MG TABLET	\$885.66	10
Label Name	Total Reimb Amt	Rx Num
FOCALIN 10 MG TABLET	\$5,846.28	118
FOCALIN 2.5 MG TABLET	\$1,287.63	58

FOCALIN 5 MG TABLET	\$6,015.55	154
Totals	13,149.46	330
Label Name	Total Reimb Amt	Rx Num
FOCALIN XR 10 MG CAPSULE	\$32,798.56	360
FOCALIN XR 15 MG CAPSULE	\$5,009.95	46
FOCALIN XR 20 MG CAPSULE	\$34,004.14	372
FOCALIN XR 5 MG CAPSULE	\$20,022.37	228
Totals	\$91,835.02	1006
Label Name	Total Reimb Amt	Rx Num
METADATE CD 10 MG CAPSULE	\$15,901.64	231
METADATE CD 20 MG CAPSULE	\$72,141.85	738
METADATE CD 30 MG CAPSULE	\$32,209.54	347
METADATE CD 40 MG CAPSULE	\$7,798.94	73
METADATE CD 50 MG CAPSULE	\$1,296.36	9
METADATE CD 60 MG CAPSULE	\$585.54	4
Totals	\$129,933.87	1402
Label Name	Total Reimb Amt	Rx Num
METADATE ER 20 MG TABLET SA	\$184.60	5
Label Name	Total Reimb Amt	Rx Num
METHYLIN 10 MG TABLET	\$20,594.75	964
METHYLIN 10 MG/5 ML SOLUTION	\$1,039.83	21
METHYLIN 20 MG TABLET	\$15,070.19	472
METHYLIN 5 MG TABLET	\$9,086.20	522
Totals	\$45,790.97	1979
Label Name	Total Reimb Amt	Rx Num
METHYLIN ER 10 MG TABLET SA	\$2,466.47	90
METHYLIN ER 20 MG TABLET SA	\$4,320.04	161
Totals	\$6,786.51	251

Label Name	Total Reimb Amt	Rx Num
METHYLPHENIDATE 10 MG TABLET	\$6,233.79	293
METHYLPHENIDATE 20 MG TABLET	\$9,855.45	285
METHYLPHENIDATE 5 MG TABLET	\$2,003.15	118
Totals	\$18,092.39	696
Label Name	Total Reimb Amt	Rx Num
METHYLPHENIDATE ER 20 MG TAB	\$3,007.31	103
Label Name	Total Reimb Amt	Rx Num
RITALIN 10 MG TABLET	\$224.37	5
RITALIN 20 MG TABLET	\$2,969.70	23
RITALIN 5 MG TABLET	\$62.14	3
Totals	\$3,256.21	31
Label Name	Total Reimb Amt	Rx Num
RITALIN LA 10 MG CAPSULE	\$13,102.54	141
RITALIN LA 20 MG CAPSULE	\$31,629.59	407
RITALIN LA 30 MG CAPSULE	\$35,984.80	465
RITALIN LA 40 MG CAPSULE	\$38,718.25	443
Totals	\$119,435.18	1456
Label Name	Total Reimb Amt	Rx Num
RITALIN-SR 20 MG TABLET SA	\$296.40	5
Label Name	Total Reimb Amt	Rx Num
STRATTERA 10 MG CAPSULE	\$21,460.00	187
STRATTERA 100 MG CAPSULE	\$857.88	6
STRATTERA 18 MG CAPSULE	\$26,016.85	245
STRATTERA 25 MG CAPSULE	\$69,640.76	635
STRATTERA 40 MG CAPSULE	\$150,878.98	1145
STRATTERA 60 MG CAPSULE	\$57,299.92	556
STRATTERA 80 MG CAPSULE	\$11,026.10	79
Totals	\$337,180.49	2853

Utilization by Cost

Label Name	Total
Concerta	\$665,913.57
Adderall XR	\$526,235.00
Strattera	\$337,180.49
Metadate CD	\$129,933.87
Ritalin LA	\$119,435.18
Focalin XR	\$91,835.02
Amphetamine Salts	\$75,520.38
Methylin	\$45,790.97
Daytrana	\$37,110.06
D-Amphetamine	\$29,992.51
Methylphenidate	\$18,092.39
Focalin	\$13,149.46
Adderall	\$11,242.67
Dextroamphetamine	\$9,664.85
Methylin ER	\$6,786.51
Ritalin	\$3,256.21
Methylphenidate ER	\$3,007.31
Dexedrine Spansule	\$2,667.01
Dextrostat	\$885.66
Ritalin SR	\$296.40
Dexedrine	\$250.50
Metadate ER	\$184.60

Utilization by Duration of Therapy

Amphetamine Preparations Short-acting

Amphetamine Salts	\$75,520.38
Adderall	\$11,242.67
Dextroamphetamine	\$9,664.85
Dextrostat	\$885.66
Dexedrine	\$250.50

Amphetamine Preparations Intermediate-acting

D-Amphetamine SA	\$29,992.51
Dexedrine Spansule	\$2,667.01

Amphetamine Preparations Long-acting

Adderall XR	\$526,235.00
-------------	--------------

Methylphenidate Preparations Short-acting

Methylin	\$45,790.97
Methylphenidate	\$18,092.39
Focalin	\$13,149.46
Ritalin	\$3,256.21

Methylphenidate Preparations Intermediate-acting

Metadate CD	\$129,933.87
Ritalin LA	\$119,435.18
Methylin ER	\$6,786.51
Methylphenidate ER	\$3,007.31
Ritalin SR	\$296.40
Metadate ER	\$184.60

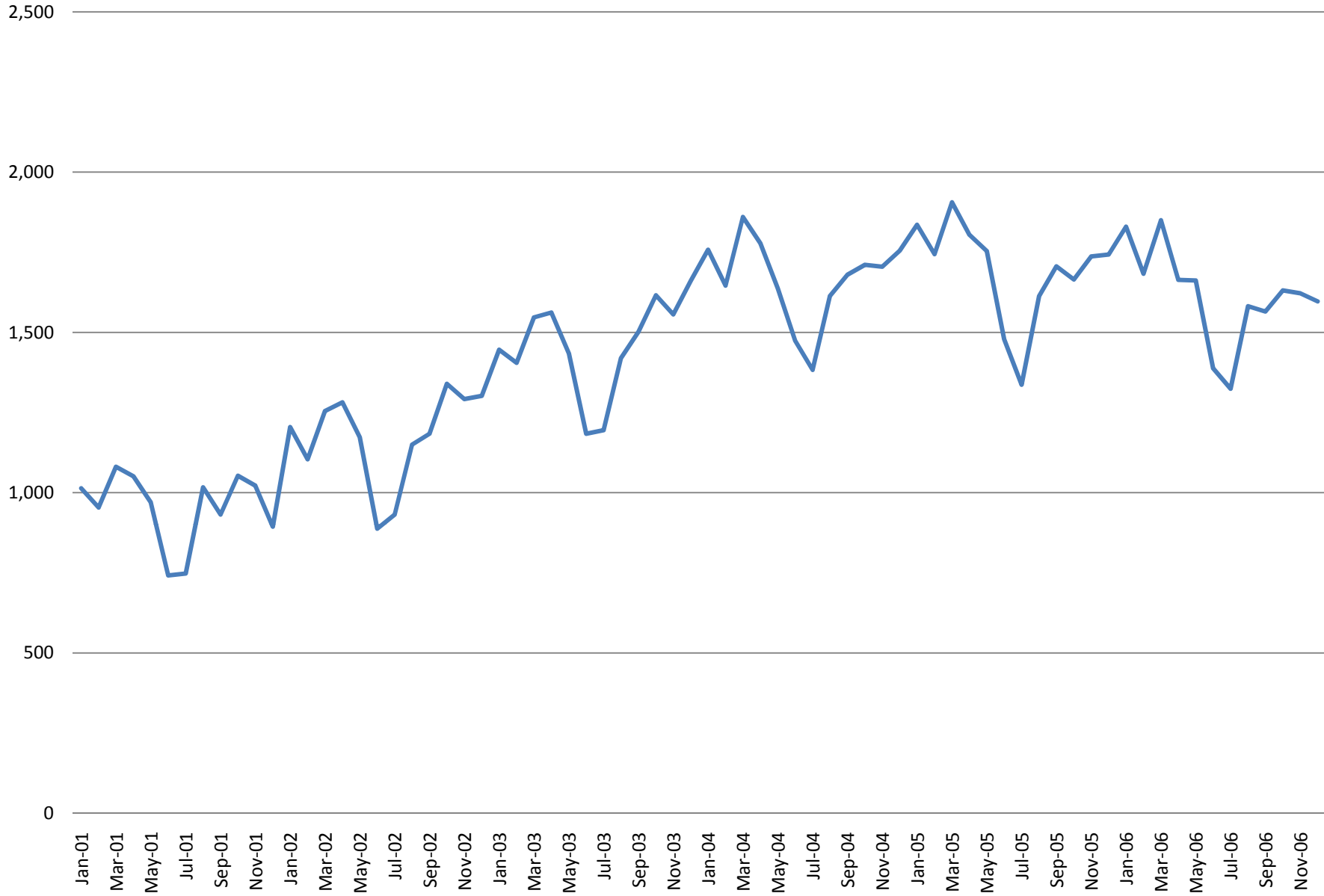
Methylphenidate Preparations Long-acting

Concerta	\$665,913.57
Focalin XR	\$91,835.02
Daytrana	\$37,110.06

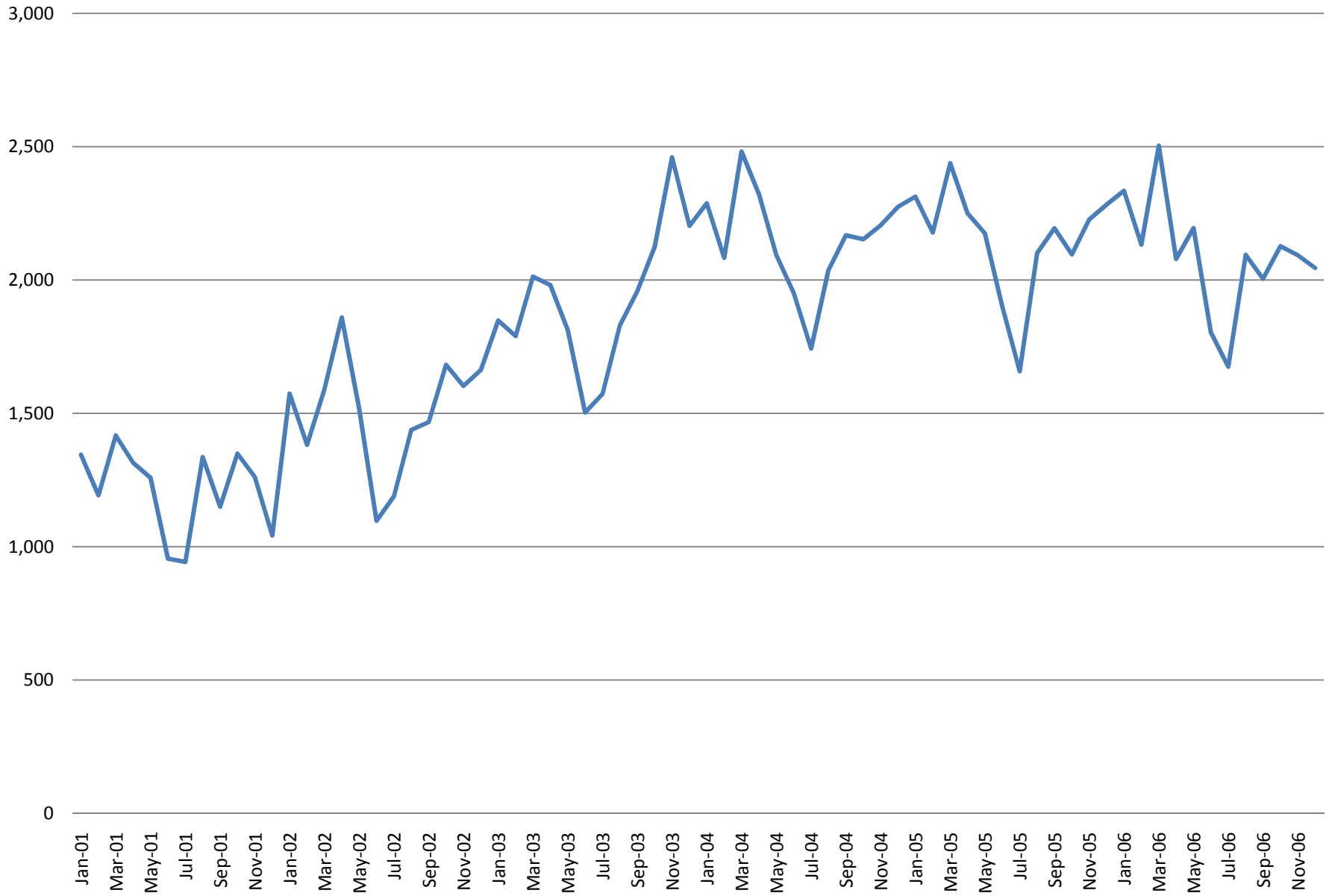
Selective Norepinephrine Reuptake Inhibitor

Strattera	\$337,180.49
-----------	--------------

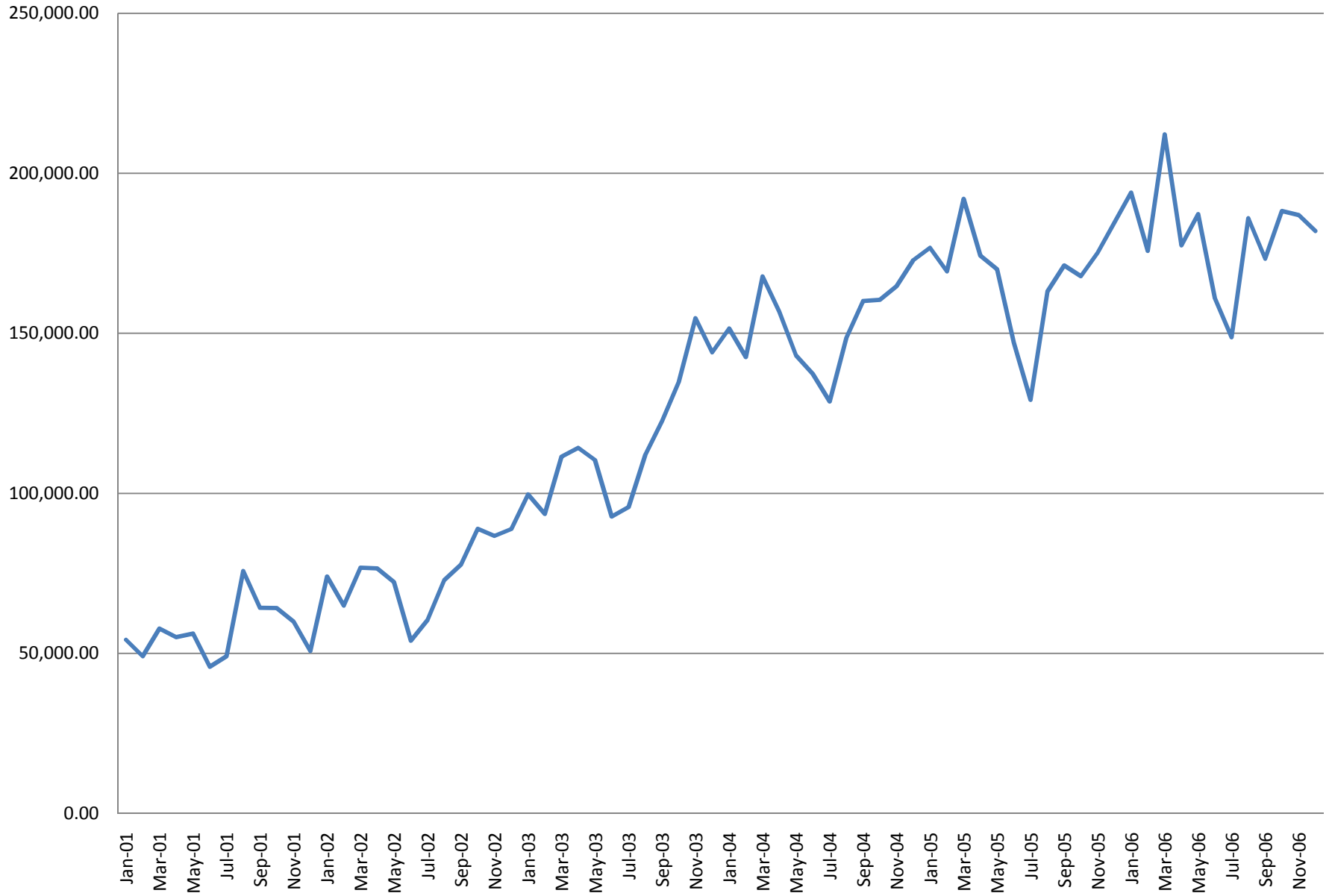
ADHD TOTAL RECIPIENTS



ADHD TOTAL RXS



ADHD CLAIMS COST





VYVANSE PA FORM

**Fax Completed Form to:
866-254-0761
For questions regarding this
Prior authorization, call
866-773-0695**

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients try and fail Adderall XR or amphetamine Salts.

***Note:**

- **Adderall XR and amphetamine salts do not require a PA**

Part I: TO BE COMPLETED BY PHYSICIAN

RECIPIENT NAME: Recipient Date of birth: / /		RECIPIENT MEDICAID ID NUMBER:
PHYSICIAN NAME:		PHYSICIAN MEDICAID ID NUMBER:
Address:		Phone: ()
City:		FAX: ()
State:	Zip:	
REQUESTED DRUG:	Requested Dosage: (must be completed)	
Qualifications for coverage:		
<input type="checkbox"/> Abuse of Adderall or amphetamine salts	Start Date:	Dose:
	End Date:	Frequency:
Physician Signature:		Date:

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:	ND MEDICAID PROVIDER NUMBER:
Phone:	FAX:
Drug:	NDC#:

Part III: FOR OFFICIAL USE ONLY

Date: / /	Initials: _____
Approved - Effective dates of PA: From: / /	To: / /
Denied: (Reasons)	

North Dakota Department of Human Services Vyvance Authorization Algorithm

