

Wyoming Drug Utilization Review

Attention Deficit Hyperactivity Disorder (ADHD)

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ADHD is characterized by excessive motor activity, impulsiveness, and difficulty in maintaining attention. ADHD causes impairment in daily function, is noticeable in two or more settings, and is not caused by another mental disorder. Children with ADHD may present with inattention, hyperactivity, impulsivity, academic underachievement, or behavioral problems. ADHD is most prevalent in ages 6 to 12 years and affects about 9% of children.¹ Approximately 60% of children do not grow out of ADHD and present with modified forms of ADHD throughout adulthood.^{1,2} Most adults present with less hyperactivity and impulsivity than children.

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Diagnosing children with ADHD requires the utilization of the DSM-IV criteria along with direct supporting evidence from caregivers, parents, and classroom teachers.^{3,4,5} The DSM-IV criteria defines three different types of ADHD: ADHD-primarily inattentive, ADHD-primarily impulsive/hyperactive, and ADHD-combined type.⁴ ADHD-inattentive type is commonly referred to ADD, because the symptoms are mainly attention difficulties instead of hyperactivity and impulsivity.⁶ ADHD-impulsive/hyperactive type presents primarily with hyperactivity and impulsivity instead of attention difficulties.⁶ Patients with inattentive and impulsive/hyperactive type symptoms have ADHD-combined type.⁶

Stimulant therapy is usually considered first-line in the treatment of ADHD.⁶ The mechanism of action varies between stimulants. They can enhance the release of dopamine and norepinephrine from presynaptic neurons, inhibit the reuptake of dopamine and norepinephrine, or inhibit monoamine oxidase. Stimulant products include dexamethylphenidate, methylphenidate, dextroamphetamine, and amphetamine mixed salts.

In Wyoming and across the nation, methylphenidate is the active ingredient most commonly found in treatment interventions.^{2,7,8} Table 1 and Table 2 on page 3 report data for prescribing patterns in Wyoming.⁸ Methylphenidate blocks dopamine reuptake into the central nervous system's presynaptic neurons. The majority of methylphenidate products are racemic mixtures, with both d- and l-threo enantiomers. Products containing the d-threo methylphenidate enantiomer only are Focalin and Focalin-XR (dexmethylphenidate).⁷

Short-acting methylphenidate preparations, such as Ritalin and Methylin, are immediately released and rapidly absorbed. Single-pulse, or intermediate-acting, medications include Ritalin SR, Metadate ER, and Methylin ER. These sustained-release capsules utilize a waxy matrix to prolong release of methylphenidate. Metadate CD, Ritalin LA, and Focalin XR are beaded, double-pulse, long-acting methylphenidate products. The beaded, double-pulse has a bi-modal release mechanism resulting in an extended-release formulation. Concerta is an osmotic-release, long-acting methylphenidate. The dose is delivered through an osmotic pump, gradually releasing the drug over 10 hours. Daytrana is a transdermal, long-acting methylphenidate patch.^{7,9} Long acting preparations make up the bulk of claims filed in Wyoming, with Concerta accounting for the highest amount of expenditures.⁸

Amphetamines are available in a racemic and d-isomer form. Dextrostat and Dexedrine are dextroamphetamines consisting of only the d-amphetamine isomer, while Adderall and Adderall XR are mixtures of d- and l-amphetamine. Dextroamphetamine is as effective as methylphenidate when treating ADHD related overactivity, impulsivity, and inattention.⁷ If a patient does not respond to methylphenidate, an amphetamine may be an alternative and vice versa.⁷ Adderall XR is a double pulse capsule that contains immediate and extended release beads. In the Wyoming Medicaid population, Adderall XR is the most commonly prescribed amphetamine product.⁸

If patients fail first-line options, second-line agents such as atomoxetine, bupropion and tricyclic antidepressants (TCAs) are available. In comparison to stimulants, these medications provide a lower potential for sleep disturbances, risk of abuse, and appetite suppression.

Atomoxetine (Strattera) is the first non-stimulant approved by the Food and Drug Administration (FDA) to treat ADHD. Strattera is a selective norepinephrine reuptake inhibitor and is not a controlled substance. On average, two to four weeks are necessary to see an effect, versus one hour with a stimulant.

When compared to stimulants, anti-depressants have a more continuous and sustained improvement of ADHD associated symptoms.² Bupropion is a dopamine and norepinephrine

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WY-DUR Board Meeting Update

The DUR Board met for its bimonthly business meeting on March 27, 2008. Highlights of this meeting include:

- The DUR Board approved the following recommendations from the Psychiatry Advisory Board for the antiepileptic criteria.
 1. Add unspecified mood disorder to lamotrigine and oxcarbazepine.
 2. Delete major depressive disorder from lamotrigine and oxcarbazepine (these were never intended to be included).
 3. Add schizoaffective disorder to lamotrigine only.

- The Board agreed to change the preferred insomnia agents to zolpidem and Lunesta. Sonata will be deleted from preferred status.
- Baclofen will be made a preferred agent in the skeletal muscle relaxant class.

The next DUR Board meeting will be held May 29, 2008 in Casper. Topics for discussion will include a review of asthma utilization, newly approved medications and the mandatory generic policy in regards to Zonegran and Trileptal. An agenda will be posted approximately two weeks prior to the meeting.

Tamper Resistant Rx Pads

Attention Wyoming EqualityCare Pharmacy Providers – Important Information

Section 7002(b) of the U.S. Troop Readiness, Veterans' Care, Katrina Recovery and Iraq Accountability Appropriations Act of 2007 requires that ALL written, non-electronic prescriptions for EqualityCare outpatient drugs be executed on tamper resistant pads in order for them to be reimbursable by the federal government. In addition to all current Wyoming Board of Pharmacy requirements for Tamper Resistant prescription forms, all prescriptions paid for by EqualityCare must meet the following requirements to meet standards set forth in this law and to decrease tampering to the greatest extent possible at this time.

Written prescriptions:

As of April 1, 2008 must contain one, and as of October 1, 2008, must contain all three of the following characteristics:

1. One or more industry-recognized features designed to prevent unauthorized copying of a completed or blank prescription form. In order to meet this requirement all written prescriptions must contain:
 - Some type of "void" or "illegal" pantograph that appears if the prescription is copied.
 - May also contain any of the features listed within category one or that meets the standards set forth in this category.
2. One or more industry-recognized features designed to prevent the erasure or modification of information written on the prescription by the prescriber. In order to meet this requirement all written prescriptions must contain:
 - Quantity check-off boxes, or alpha AND numeric forms of all quantity values.
 - Refill Indicator (circle or check number of refills or "NR") or alpha AND numeric forms of all refill values.
 - May also contain any of the features listed within category two or that meets the standards set forth in this category.

3. One or more industry-recognized features designed to prevent the use of counterfeit prescription forms. In order to meet this requirement all written prescriptions must contain:
 - Security features and descriptions listed on the FRONT of the prescription blank.
 - May also contain any of the features listed within category three or that meets the standards set forth in this category.

Computer Printed Prescriptions:

Computer printed prescriptions must meet the same standards outlined for written prescriptions above for requirements 1 and 2. The 3rd requirement differs as follows:

- One or more industry-recognized features designed to prevent the use of counterfeit prescription forms. In order to meet this requirement all prescriber's computer generated prescriptions must contain:
- Security features and descriptions listed on the FRONT *or* BACK of the prescription blank.
 - May also contain any of the features listed within category three or that meets the standards set forth in this category.

Inclusion of other industry recognized features on a prescription are acceptable if desired, however, the above features will be mandatory for all prescriptions paid for by EqualityCare as of the dates referenced above.

The tamper-resistant requirement does not apply when a prescription is communicated by the prescriber to the pharmacy electronically, verbally, or by fax; when a managed care entity pays for the prescription; or in most situations when drugs are provided in designated institutional and clinical settings. The guidance also allows emergency fills with a non-compliant written prescription as long as the prescriber provides a verbal,

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reuptake inhibitor, monocyclic anti-depressant. Bupropion is dosed 50-300 mg daily and has less overdose potential than TCAs. TCAs are not as effective as stimulants for increasing attention, but control hyperactivity and impulsivity.⁶ TCAs used for the treatment of ADHD include desipramine, imipramine, and nortriptyline. These are dosed 50-150 mg daily.

Other medications, including antihypertensive agents, anticonvulsants, antipsychotics, modafinil, and donepezil, have been used off-label in ADHD treatment with various levels of supporting evidence. The antihypertensive agent clonidine, and less often guanfacine, are less effective than stimulants in treatment of ADHD, and are usually prescribed as adjunct therapy. Anticonvulsants such as lithium, carbamazepine, and valproate are being used to increase the control of aggression and explosive behavior in ADHD. Antipsychotics such as risperidone (Risperdal), olanzapine (Zyprexa), quetiapine (Seroquel), and ziprasidone (Geodon) have shown to improve symptoms of impulsivity and hyperactivity. However, the resulting negative effects on learning and cognitive function limit their usefulness.⁶ Modafinil (Provigil) and donepezil (Aricept) have also been used off-label to treat patients with ADHD.⁷ One study found that Aricept may not be useful and is not well tolerated in the treatment of patients with residual ADHD.¹⁰

Health professionals can help by counseling and guiding children and adults with ADHD to develop new techniques to cope with their disease. Through individual counseling, therapists can help children feel better about themselves, identify and build on their strengths, and control their attention and aggression. Such interventions include psychotherapy, behavioral therapy, social skills training, support groups, and parental skills training.¹¹

Frustrating situations may arise for patients with ADHD and those around them. Patients may find ways to handle their disorder on their own. Often, these coping techniques are not enough and patients will ultimately struggle with symptoms. With the addition of pharmacologic therapy, such as stimulants and second-line treatments, alleviation of symptoms and less functional impairment may result for patients with ADHD. Treatment

adjuncts, such as behavioral ADHD therapy, allow patients to improve their social and academic functioning. Through careful titration and combinations of treatment methods, ADHD becomes manageable for the patient and family.

References

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Tamper Resistant Rx Pads

faxed, electronic, or compliant written prescription within 72 hours.

The Board of Pharmacy's website, under "Items of Interest from the Board" has a section on security paper and a listing of approved vendors. Please contact vendors directly for information on security features of their products. Audits of pharmacies will be performed in the future by the Wyoming Department of Health, Program Integrity Unit to ensure that the above requirement is being followed. If you have any questions about these audits or this regulation, please contact the Wyoming Department of Health, Office of Pharmacy Services (OPS) at 1-800-438-5785 or visit the OPS website at the following address: www.health.wyo.gov/healthcarefin/pharmacy.

Table 1: Prescription Numbers

Active Ingredient	Number of Prescriptions
Methylphenidate/Dexmethylphenidate	12,964
Amphetamine/Dextroamphetamine	6,385
Atomoxetine	5,233

Table 2: Prescription Dollars

Active Ingredient	Dollars Spent
Methylphenidate/Dexmethylphenidate	\$1,420,159
Amphetamine/Dextroamphetamine	\$687,037
Atomoxetine	\$742,331

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